
# NAVAL POSTGRADUATE SCHOOL

**MONTEREY, CALIFORNIA**

# THESIS

**ANALYZING PREDICTORS OF HIGH OPIOID USE IN THE U.S. NAVY**

by

Francis Tam

September 2016

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The study concludes that a simple, executable model that consolidates the variables to two explanatory factors performs as well, if not better than, the more complicated machine learning models. The two highly influential factors are the number of prescription sources for opioid medications and the total number of diagnoses.

This logistic regression model has the potential to benefit Navy Medicine to make important decisions for their opioid-prescribed patients. With the ability to identify the risk that an opioid user becomes a high user, healthcare leaders can better manage resources to focus on the prevention and treatment of higher-risk patients. This concentrated coordination can result in improved patient care for this sub-population, reduced long-term cost for the military healthcare system and, overall, a more medically ready military force.

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# ANALYZING PREDICTORS OF HIGH OPIOID USE IN THE U.S. NAVY

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# LIST OF ACRONYMS AND ABBREVIATIONS

| | |
|---|---|
| AD | active duty |
| BJMIN | bone/joint/muscle infections/necrosis |
| BUMED | Navy Bureau of Medicine and Surgery |
| CDC | Centers for Disease Control and Prevention |
| CI | confidence interval |
| CM | case management |
| CNA | Center for Naval Analyses |
| COU | chronic opioid user |
| EMI | endocrine/metabolic/immunity disorders |
| FY | fiscal year |
| ID | identification |
| Lasso | least absolute shrinkage and selection operator |
| LRT | likelihood ratio test |
| M2 | Military Health System Management Analysis and Reporting Tool |
| MCSC | managed care support contractor |
| MTF | military treatment facility |
| NIDA | National Institute on Drug Abuse |
| NMCPHC | Navy and Marine Corps Public Health Center |
| NSAID | nonsteroidal anti-inflammatory drugs |
| OCO | Overseas Contingency Operation |
| OR | odds ratio |
| PDTS | Pharmacy Detail Transaction Service |
| PTSD | post-traumatic stress disorder |
| ROC | receiver operating characteristic |
| SE | standard error |
| VA | Veterans Affairs |
| WRA | Wakely Risk Assessment |

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# EXECUTIVE SUMMARY

In an effort to build a model to identify the risk that opioid users may become high users, our study examines explanatory factors that influence opioid use. The data is provided by the Analytics/Enterprise Support Services Department of BUMED and focuses on active duty (AD) service members enrolled to the Puget Sound area Navy military treatment facilities (MTF). The analysis examines the relationship between the response variable, high opioid user, as a function of 91 explanatory variables, including patient age, deployment history, sources of prescription and medical diagnoses. Basic logistic regression, elastic net penalized logistic regression, random forest and boosted tree classification models are used for our data analysis.

We plotted cross-validated receiver operating characteristic (ROC) curves to compare model performance and to avoid over-fitting for the random forest and boosted tree models. Although simpler, the basic logistic regression model performs well when compared to the complex machine learning models. The logistic regression model is also easier to reproduce. Just as importantly, the output is easy to understand and interpret. The log-odds and probability of a high user are a linear function of the two explanatory variables in the final logistic regression model and thus, conceptually, easier to communicate.

Therefore, the recommended model for BUMED is a logistic regression model with two explanatory variables, without interactions. These two variables, the number of prescription sources for opioid medications and the total number of diagnoses are constructed from the original data files from BUMED and encompass the majority of the 91 explanatory variables.

A lift curve is used for improved interpretability of the model for decision makers. The curve shows that with limited resources, if MTFs could subset the patients, by focusing on a percentage of the opioid user population with the highest estimated probability of high opioid use, the probability of identifying a high user can be improved by the amount of the lift.

This logistic regression model has the potential to benefit Navy Medicine to make important decisions for their opioid prescribed patients. With the ability to identify the risk that an opioid user becomes a high user, health care leaders can better plan and manage finite resources to focus on the prevention and treatment of the higher risk patients. This concentrated coordination of care can result in improved patient care for this sub-population, reduced long term cost for the military health care system and overall, a more operationally ready workforce.

This research is an initial effort to explore ways to identify opioid users that may have greater risk of becoming a high opioid user. For future studies, research can also examine data on patients that did not have opioids prescribed to compare the risk factors of becoming an opioid user.

# ACKNOWLEDGMENTS

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# I. INTRODUCTION

In the United States, there is a growing epidemic that until recently has not received much media coverage: the use of opioids to relieve pain. Opioids are a type of narcotic, commonly prescribed for pain. Roughly 20% of patients with pain-related diagnoses are prescribed an opioid (Chou, Dowell, & Haegerich, 2016). According to the National Institute on Drug Abuse (NIDA), opioids can be natural, semisynthetic or synthetic. The drugs provide relief by reducing the intensity of pain signals to the brain and this, in turn, minimizes the effects of the painful stimulus (NIDA, 2014). Some common medications that are considered opioids include hydrocodone, oxycodone, morphine and codeine (NIDA, 2014).

Opioid pain medications can present serious risks for the patient, including dependency, overdose and opioid-use disorder. Opioid abuse has become the leading cause of preventable deaths in the United States (Rudd, Aleshire, Zibbell, & Gladden, 2016). In 2014 alone, according to the same source, there were over 47,000 deaths attributed to drug overdose and 61% of those deaths involved opioid overdoses. That is roughly 25% more deaths than from either firearms or motor vehicle accidents. The Centers for Disease Control and Prevention (CDC) has historically characterized all opioid pain reliever deaths as prescription opioid overdoses (Rudd et al., 2016). Additionally, the numbers continue to dramatically increase; Figure 1, taken from a CDC (2015) report, shows that the rate of opioid overdoses has tripled since 2000. This increase is alarming and present in all demographics, regardless of sex, age or race (Rudd et al., 2016). The focus of this study is a specific population of opioid users, active duty (AD) military personnel.

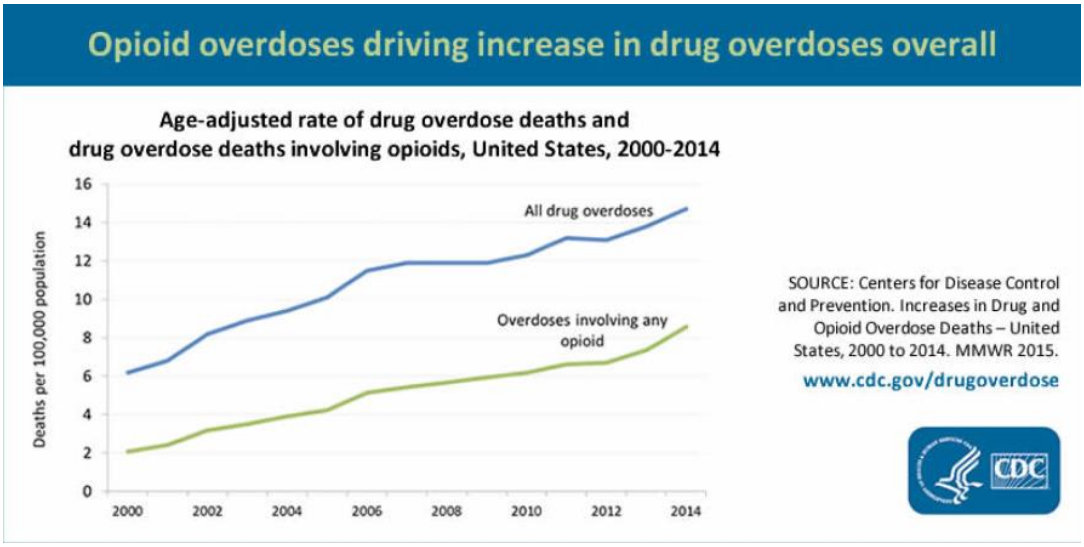


Figure 1. Overdose Death Rates from 2000–2014. Source: CDC (2015).

## A. BACKGROUND

Several important factors contribute to the increase in opioid use and abuse. The liberalization of laws governing the treatment of chronic pain, the aggressive marketing efforts of the pharmaceutical industry and the introduction of a different pain management standard that began in the 1990s have all played major roles. Prior to 1990, U.S. physicians took a minimalist approach to treating chronic pain patients (Levy, Netzer, & Pikulin, 2014).

In 2015, the CDC published suggested guidelines for prescribing opioids for chronic pain in the United States (Chou et al., 2016). These guidelines specifically focus on affecting medical provider's behavior to ensure the safest and most effective treatment for their patients. The guidelines also discuss the use of opioids in treating chronic pain. The guidelines do not target treatment of patients with cancer, palliative care or end-of-life type care. Instead, they are intended for primary care providers, who treat chronic-pain patients in outpatient settings, as they account for almost half of all opioid prescriptions. Chou et al. (2016) noted that the recommendations are based on three key principles. The first is that non-opioid therapy is the preferred method for chronic pain treatment. The second is that the lowest possible opioid dosage should be selected to

reduce risk of overdose. Thirdly, providers should always exercise caution when prescribing opioids while closely monitoring their patients.

Opioid abuse is not just a problem for the civilian population. It is a problem for our nation's military personnel and veterans as well. According to a Veterans Affairs (VA) study, veterans are twice as likely to die from accidental opioid overdose than non-veterans (Childress, 2016). Additionally, Childress (2016) noted, that more than half of veterans suffer from chronic pain, compared to only about 30% for the general population, where chronic pain is defined "as pain that lasts longer than three months or past the time of normal tissue healing." Until a few years ago, veterans with chronic pain were treated exclusively with opioids. The prevention, assessment and treatment of chronic pain remain a tremendous challenge for health care providers (Childress, 2016). The Navy AD population is on average much younger than the general population. Nevertheless, in a recent Center for Naval Analyses (CNA) study of four large Navy military treatment facilities (MTF), roughly 25% to 32% of all AD beneficiaries received at least one opioid prescription during fiscal year (FY) 2013 (Levy et al., 2014).

The United States Navy Bureau of Medicine and Surgery (BUMED) stresses in its vision statement "our health care is patient-centered and provides best value, preserves health, and maintains readiness" (Goff & Sayers, 2015). Thus, two of BUMED's three strategic principles are value and readiness. More specifically, under the value principle, the goal is to decrease enrollee network cost by optimizing resource utilization and managing referrals in order to provide the best care at the best value. Under the readiness principle, the goal is to deliver ready capabilities to the operational commander by aligning Navy Medicine's "manning, training, and equipping to maintain a medically ready force (Goff & Sayers, 2015)."

According to Levy et al. (2014), around 80% of health care resources for Navy beneficiaries are devoted to patients with chronic pain. Since chronic pain patients are typically prescribed opioids, this group drives a disproportionate amount of the populations cost to the health care system. Additionally, from an operational and readiness standpoint, the Navy may not be able to deploy patients who have been prescribed opioids for chronic pain or those that have many of the associated comorbid

conditions. Thus, the need to identify and manage the high opioid user population is one of strategic importance that aligns with BUMED's strategic principles of value and readiness.

## B. PURPOSE OF THE STUDY

High opioid use is defined by the Navy and Marine Corps Public Health Center (NMCPHC) as having five or more prescriptions dispensed for select pain medications within 90 days (Broad, 2016). Identifying a potential high opioid user early will allow health care professionals and leaders to more closely monitor this group of beneficiaries to ensure they receive comprehensive care while mitigating the cost and operational impact on the patient's parent organization.

This study examines over eighty demographic and patient medical variables for opioid users in an AD military population and builds a simple logistic regression model to estimate the probability an opioid user from this population is a high opioid user. While this model is not good for classifying a particular individual as a high opioid user, we show that it can be used to identify the increase in the concentration of high users in a smaller sub-population. We also show that the simple model performs well or better than more complex machine learning models (penalized logistic regression, random forests, boosted trees) fit with the same data. The results of this study can be used by BUMED to help achieve its strategic goals in the areas of readiness and value.

## C. ASSESSING AND DEFINING HIGH OPIOID USERS AMONG AD NAVY POPULATION

Across different health care systems, multiple methodologies and definitions are used for patients treated for chronic pain. In 2015, BUMED established a comprehensive case definition to assess and identify opioid-prescribed patients enrolled in Navy MTFs. The adopted definition for a high opioid user is the same as NMCPHC's definition of five or more dispensing events of a medication likely to be associated with pain during the course of a 90-day period (Ellis, 2015). The types of medication that would fall within this category are listed below to include certain therapeutic classes and selected

nonsteroidal anti-inflammatory drugs (NSAID) likely to be associated with pain (Ellis, 2015).

- Opiate Agonists
- Opiate Partial Agonists
- Skeletal Muscle Relaxants
- Centrally Acting Skeletal Muscle Relaxants
- Direct-Acting Skeletal Muscle Relaxants
- Gaba-derivative Skeletal Muscle Relaxants
- Skeletal Muscle Relaxants, Misc.
- Selected NSAIDS (Aspir, Celecoxib, Ketoro, Cambia, Rub, Sulindac)

Based on those medications, BUMED extracted administrative medical data and the Pharmacy Detail Transaction Service (PDTS) data from the Military Health System Management Analysis and Reporting Tool (M2). The data only includes AD service members with at least one opioid prescription in FY2014 or FY2015 who were enrolled to the Puget Sound area Naval MTF's. These are the five facilities:

- Naval Hospital Bremerton
- Naval Hospital Oak Harbor
- Naval Branch Health Clinic Everett
- Naval Branch Health Clinic Bangor
- Naval Branch Health Clinic Puget Sound

Patients diagnosed with any of the cancer-related codes were excluded from the high opioid user criteria and removed from the PDTS data. Appendix A lists the codes associated with cancer diagnosis. This group of patients are already closely monitored and specifically prescribed opioids for their cancer-induced pain. Based on the pseudo-identification (ID) code representing each member in the PDTS data, BUMED provided a risk data file that contained additional information about each particular patient. The details of each field will be discussed in Chapter III. Due to the Health Insurance

Portability and Accountability Act of 1996, that specifically deals with protected health information as well as personally identifiable information, much of the demographic information was removed from the data files. There are a few limitations with this study.

- Reporting errors due to improper or insufficient medical coding as well as data entry errors at the clinic may exist in M2 data. Furthermore, care delivered in the operational setting may not be documented in this system.
- The PDTS table includes data for all prescriptions dispensed by an MTF, civilian pharmacy, or mail order. It cannot be determined if the patient was compliant with taking the medication as instructed.
- Patients with cancer diagnoses that did not occur at the same time as their pain diagnosis could be included in this analysis.
- Potential high opioid users that have changed enrollment sites during the FY2014 or FY2015 time period may not be detected as a high user.
- Since the reporting period covers 24 months, patients that receive opioid prescriptions outside of this period will not be accounted for.

## D. THESIS ORGANIZATION

Chapter II provides background information on high opioid users, chronic opioid users (COUs), and the connection between pain and opioids. Chapter III provides descriptive statistics of variables used in the study and gives the details of data preparation. Chapter IV explores the methodologies used, a description and assessment of the models and the results of the analysis. The final chapter presents a summary of the study and offers recommendations for further analysis.

# II. RELATED LITERATURE

This chapter examines previous studies on patients identified as high and COUs. Additionally, we explore the relationships between a very specific patient group, the military population and opioid use. By examining the common factors amongst this patient group, we hope to gain a better insight on possible predictors for AD sailors who may become high opioid users.

## A. HIGH OPIOID USERS

According to the Institute of Medicine, pain is recognized as a significant public health problem in America with over 100 million people experiencing chronic pain (Levy et al., 2014). The treatment of chronic pain is especially challenging for health care professionals. Due to its complex condition, chronic pain can be defined in different ways. According to the same source, chronic pain is defined as lasting for "greater than three months or past the time of normal tissue healing" and can result from previous medical conditions, injuries or unknown causes. An analysis in 2012 by the National Health Interview Study showed that 11.2% of adults reported having daily pain (Chou et al., 2016). In fact, Chou et al. noted that approximately one in three Americans will have chronic pain in their lifetime and over 80% of the chronic issues are on the neck or lower back. This source also reported that the majority of patients who experience chronic pain are also diagnosed with depression. The belief is that the ongoing pain and disability leads to frustration and eventually takes a psychological toll (Chou et al., 2016). Additionally, chronic pain in some people resulted from a traumatic event that may also trigger post-traumatic stress disorder (PTSD) ("PTSD," 2015). The same source approximates that 15% to 35% of patients with chronic pain also have PTSD. Only 2% of patients diagnosed with PTSD do not have chronic pain. Thus, PTSD and chronic pain have a very clear connection ("PTSD," 2015).

Opioids are commonly prescribed for non-cancer pain symptoms. There is always the risk of dependency, abuse and opioid use disorder, which is defined as a "pattern of opioid-use leading to clinically significant impairment" (Chou et al., 2016).

Thus, it is very important to identify and monitor patients who are considered high opioid users.

The Navy and Marine Corps Public Health Center conducted an M2 data pull in 2016 for each Navy MTF and discovered that roughly 4% of all AD Navy beneficiaries could be classified as high users (Broad, 2016). The percentage may be a little higher overall, as about 2,200 people fitting the description of high users were excluded because the last enrollment record did not classify them as AD or Navy enrollees. Table 1 lists each Navy MTF and its percentage of high opioid users.

Table 1. High Users of Chronic Pain Medication among AD Navy Enrollees. Source: Broad (2016).

| | | Metric 1A | | |
|---|---|---|---|---|
| | | Enrollees | Pain (ALL) | |
| | | N | N | % |
| **Total Navy Enrollees** | | 432,417 | 16,115 | 3.7 |
| **EAST Region** | | 244,740 | 9,804 | 4.0 |
| **WEST Region** | | 187,677 | 6,311 | 3.4 |
| **Region** | **Parent Enrollment Site** | | | |
| E | JAMES A LOVELL FHCC | 4,125 | 188 | 4.6 |
| E | NHC CHARLESTON | 8,557 | 159 | 1.9 |
| E | NHC NEW ENGLAND | 12,473 | 349 | 2.8 |
| E | NH BEAUFORT | 5,913 | 339 | 5.7 |
| E | NH CAMP LEJEUNE | 35,541 | 1,987 | 5.6 |
| E | NH GUANTANAMO BAY | 2,656 | 95 | 3.6 |
| E | NH JACKSONVILLE | 23,062 | 923 | 4.0 |
| E | NH NAPLES | 2,253 | 95 | 4.2 |
| E | NH PENSACOLA | 28,682 | 933 | 3.3 |
| E | NH ROTA | 2,155 | 84 | 3.9 |
| E | NH SIGONELLA | 6,712 | 170 | 2.5 |
| E | NHC ANNAPOLIS | 8,528 | 175 | 2.1 |
| E | NHC CHERRY POINT | 8,997 | 568 | 6.3 |
| E | NHC CORPUS CHRISTI | 4,784 | 224 | 4.7 |
| E | NHC PATUXENT RIVER | 5,630 | 208 | 3.7 |
| E | NHC QUANTICO | 11,318 | 402 | 3.6 |
| E | NMC PORTSMOUTH | 73,354 | 2,905 | 4.0 |
| W | NH BREMERTON | 14,036 | 362 | 2.6 |
| W | NH CAMP PENDLETON | 30,764 | 1,421 | 4.6 |
| W | NH GUAM-AGANA | 3,543 | 104 | 2.9 |
| W | NH LEMOORE | 7,807 | 295 | 3.8 |
| W | NH OAK HARBOR | 7,642 | 231 | 3.0 |
| W | NH OKINAWA | 16,776 | 539 | 3.2 |
| W | NH TWENTYNINE PALMS | 9,622 | 477 | 5.0 |
| W | NH YOKOSUKA | 18,589 | 382 | 2.1 |
| W | NHC HAWAII | 23,736 | 796 | 3.4 |
| W | NMC SAN DIEGO | 55,162 | 1,704 | 3.1 |

Navy and Marine Corps Public Health Center, Health Analysis Department
Source: MHS Mart (M2) DEERS and CAPER tables and MEDBOLTS system for LIMDU, FEB 2016

## B. CHRONIC OPIOID USERS

While there is evidence to support the short-term effectiveness of opioids in the reduction of pain, the evidence is not as clear for long-term use. Very few studies have examined the effectiveness of opioids with outcomes beyond 12 months. Yet, researchers estimated in 2005, that 3% to 4% of the U.S. adult population was prescribed long-term opioid therapy (Levy et al., 2014). Levy also suggested that patients that have a history of opioid prescriptions have a greater risk for overdose and opioid use disorder. Thus, COUs, generally defined as patients who have been prescribed a 90-day or greater supply of opioids, are of particular interest to BUMED and health care professionals (Levy et al., 2014).

In the CNA study of chronic opioid-use and lower-back pain among Navy beneficiaries at the four large Navy MTFs, they evaluated opioid-use in terms of episodes of use, days of supply and dosage (Levy et al., 2014). Some of the important factors quantified included the following:

- Was the patient also on anti-depressant?
- Was an NSAID attempted to relieve the pain, before the onset of opioid therapy?
- Did the patient receive drugs from other pharmacy sources in the civilian sector?

Table 2 shows the percentage of AD opioid users and the percentage of AD COUs for each of the four large Navy MTFs. A key point to note that is not depicted in the table is that, while the COU percentage amongst the AD population is low, ranging between 1.5% to 3%, the COUs among the retiree demographic ranged from 7.2% to 13.6% of total opioid users for each facility. This meant that age and military experiences are possibly highly influential factors.

Table 2. Percentage of Opioid Users and COUs for Each Facility.
Source: Levy et al. (2014).

| | AD |
|---|---|
| **Population** | 60,060 |
| **Opioid users** | |
| Number | 17,326 |
| % of population | 28.9 |
| **COUs** | |
| Number | 517 |
| % of opioid users | 3.0 |

NH Camp Lejeune

| | AD |
|---|---|
| **Population** | 56,043 |
| **Opioid users** | |
| Number | 15,496 |
| % of population | 27.7 |
| **COUs** | |
| Number | 283 |
| % of opioid users | 1.8 |

NH Camp Pendleton

| | AD |
|---|---|
| **Population** | 73,012 |
| **Opioid users** | |
| Number | 23,289 |
| % of population | 31.9 |
| **COUs** | |
| Number | 357 |
| % of opioid users | 1.5 |

NMC San Diego

| | AD |
|---|---|
| **Population** | 87,752 |
| **Opioid users** | |
| Number | 22,285 |
| % of population | 25.4 |
| **COUs** | |
| Number | 365 |
| % of opioid users | 1.6 |

NMC Portsmouth

CNA provided the following findings and recommendations relevant to this study (Levy et al., 2014).

- AD personnel are less likely to become chronic users compared to dependents and retiree patients.
- Users of anti-depressants are much more likely to be chronic users.
- Those prescribed a NSAID such as ibuprofen or aspirin initially, before being prescribed opioid therapy, are less likely to be chronic users.
- A higher percentage of COUs are chronic lower back pain patients versus patients with acute lower back pain.
- Patients who receive prescriptions entirely in the direct care system or entirely in purchased care are less likely to be COUs than those who receive prescriptions in both systems.

## C. PTSD, PAIN AND OPIOIDS

Based on recent research, there is a clear connection between chronic pain and PTSD. The VA reported that 51% of patients with chronic lower back pain also had PTSD symptoms ("PTSD," 2015). In another study, over 50% of Iraq and Afghanistan veterans diagnosed with PTSD also received one or more chronic pain diagnoses (Seal, 2014). Seal's research suggested that there is evidence that chronic pain is more prevalent in female veterans who recently returned from combat. Figure 2 compares the returning veterans from Iraq and Afghanistan that have pain diagnoses and examines whether they have no mental health diagnosis, with a mental health diagnosis (excluding PTSD) or have a PTSD diagnosis. The red bars are larger depicting the prevalence of chronic pain in those diagnosed with PTSD.

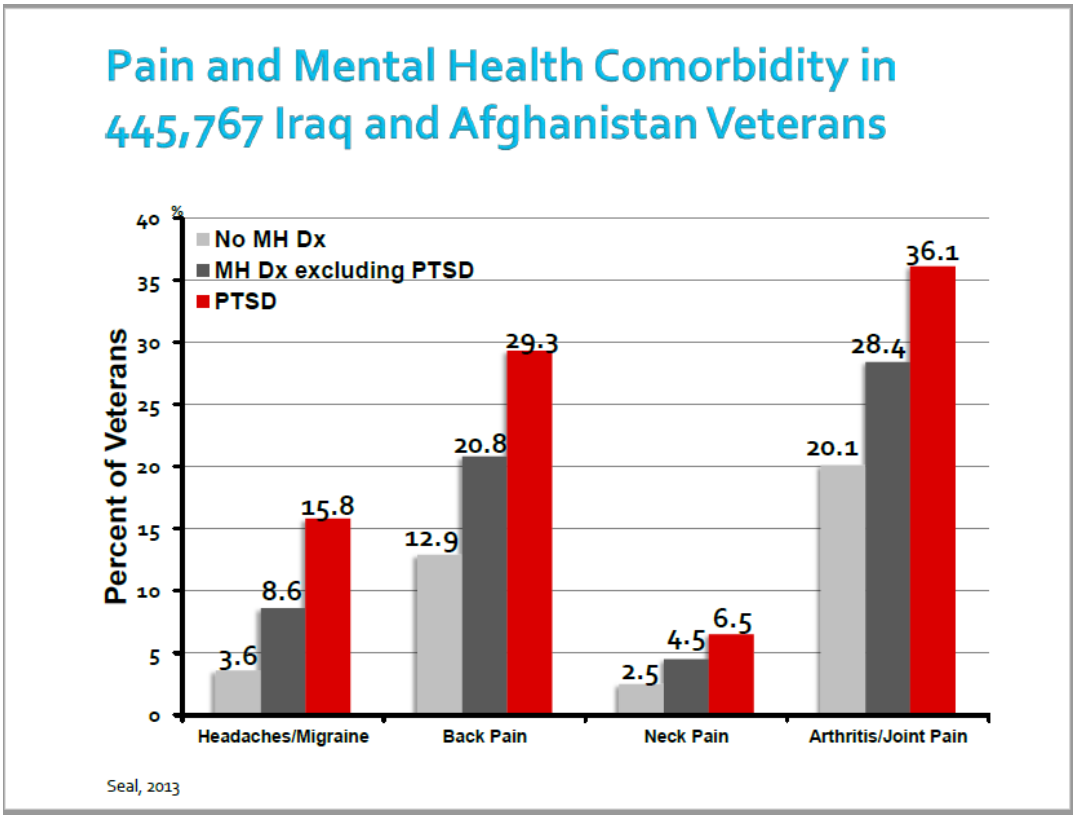


Figure 2. PTSD and Chronic Pain. Source: Seal (2014).

There are several medical hypotheses for the link between PTSD and pain. Seal presents a very compelling theory of mutual maintenance. Because PTSD creates an anxiety state, the person's pain perception is increased. As the perception of pain is exacerbated, into possibly chronic pain, this leads to increased disability. This, in turn, drives the person to perceive their pain to be even worse, which feeds back into the symptoms of PTSD. Figure 3 illustrates this cycle.

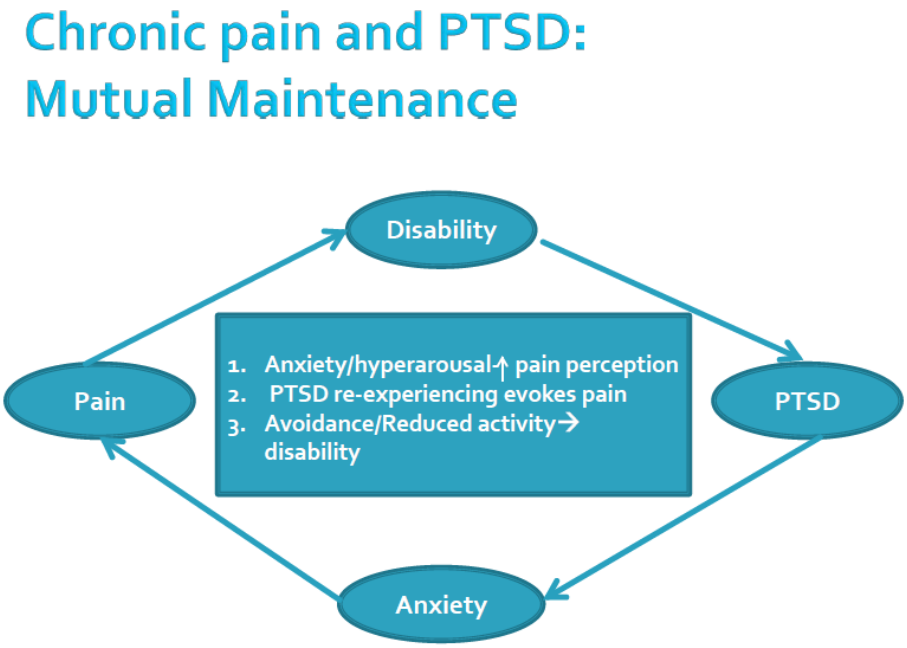


Figure 3. The Mutual Maintenance Cycle. Source: Seal (2014).

Thus, a logical follow-on is to examine the link between PTSD and opioid use. Seal's presentation (2014) references research that shows patients with both pain and PTSD are more likely to be prescribed opioids than patients with pain but no PTSD diagnosis. In her study of Iraq and Afghanistan veterans, she found that those with PTSD are over two and half times more likely to be prescribed opioids than those patients with no mental health diagnosis. Additionally, Seal concluded that of the PTSD diagnosed veterans, those with severe PTSD symptoms are more likely to receive prescription opioids for their pain. This conclusion places this group of patients into an even greater risk of adverse effects from opioid use.

# III. DATA

This chapter describes the data set analyzed in the study, the data preparation process and the description of the response and explanatory variables with some initial exploratory analysis. The variables described in this chapter are used in Chapter IV to construct models to estimate the probability that an individual in the AD military sub-population who has been prescribed an opioid at least once, is a high opioid user.

The response variable, constructed from the data provided and described in this chapter is a binary variable indicating whether an individual is a high user of opioids or not a high user of opioids, but all individuals in the data studied have at least one prescription for opioids.

There are 91 explanatory variables available directly from the data provided by BUMED. They can be categorized into three types:

- Eighty binary medical risk diagnoses (given in Appendix B) variables indicating whether the individual has or has not been diagnosed with the condition.
- Five binary variables assigning prescription source as direct care, managed care support contractor, theater medical data store, TRICARE mail-order pharmacy and VA clinical/health data repository.
- Six variables pertaining to the patient's history that may have an influence on the patient's opioid-use.

The response and explanatory variables are discussed in greater detail in Section C of this chapter. Additionally, a brief description and statistics on some of the explanatory variables is included in Section D.

## A. DATA SOURCE/CLEANING

The data used for this study was obtained from BUMED Analytics/Enterprise Support Services Department. The data contains information on AD patients assigned to Puget Sound area Naval MTF's that received at least one opioid prescription in either FY2014 or FY2015. The data was received in the form of two files, one for each fiscal

year. Each file contains two spreadsheets, one with PDTS records and one containing the patient risk file.

The PDTS spreadsheets have 7066 rows and 8066 rows for FY2014 and FY2015 respectively. Each row corresponds to a single opioid prescription issued in that year. The PDTS spreadsheets have three relevant fields:

- Pseudo ID
- Opioid issue date
- Source of opioid

Each patient is identified by their pseudo ID, assigned by BUMED to ensure patient confidentiality. The response variable and the five binary variables assigning a prescription source are constructed from this file.

The risk spreadsheets have 2889 rows for FY2014 and 3742 rows for FY2015. Each row corresponds to a patient who had at least one opioid prescription issued in that year. There were 57 duplicate pseudo IDs for the FY2014 risk file and 48 duplicate pseudo IDs for the FY2015 risk file. The files contain 86 fields for the explanatory variables (including the 80 medical diagnosis fields plus six others) and a field containing the ID.

Each of the four spreadsheets are exported to comma separated value files and imported into the R programming environment for further manipulation (R Core Team, 2016). The two PDTS files are combined before constructing the high user response variable based on BUMED's definition. Specifically, we define a high user to be any patient who is prescribed five or more opioids within 90 days based on the combined two-years of PDTS records. From the combined PDTS files, we construct a single PDTS user output file with one row per unique pseudo ID and columns for pseudo ID, the minimum number of days between any sequence of five prescriptions for individuals with at least five prescriptions, and a column denoting whether the patient was a high user. Figure 4 shows a histogram of the minimum number of days between a sequence of five opioid prescriptions, for each patient who has five or more prescriptions. The figure shows that only 649 patients have five or more prescriptions and only 235

patients, highlighted in red, have five or more prescriptions within a 90 day period accounting for 11.4% and 4.1% respectively, of the total patients in the data set.

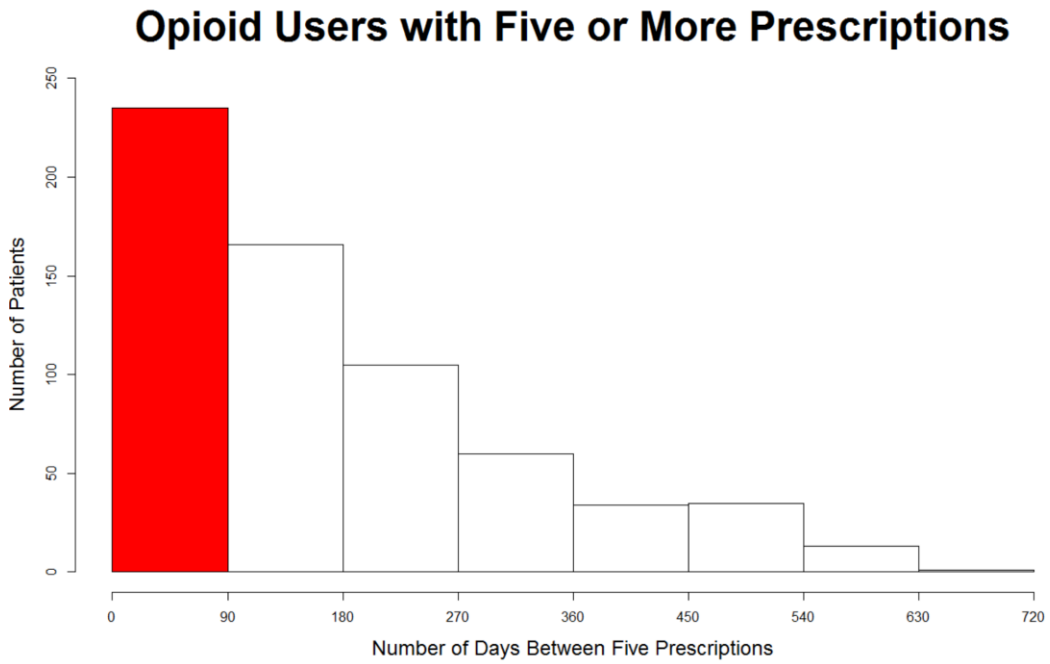


Figure 4. A Histogram of the Minimum Number of Days between a Sequence of Five Opioid Prescriptions among Opioid Users with at Least Five Prescriptions in FY2014 and FY2015

The two risk files are combined and then merged with the PDTS user output file based on pseudo IDs. An additional column is added to annotate the fiscal year (FY2014 or FY2015) of the source risk file. The newly combined output file contains 6,631 entries with some pseudo IDs appearing multiple times. This file is then separated by fiscal year. Duplicate ID's within each fiscal year are merged, with the patient assuming the larger value for each explanatory variable. For example, if the pseudo ID appeared three times in FY2014, with one entry having a risk score of one and another entry with a risk score of two and the third with a risk score of three, the updated file would contain the pseudo ID once, with a risk score value of three. The higher value is adopted to assume a worse case patient characteristic. This decreases the size of the FY2014 and FY2015 files to 2,831 and 3,692 patients respectively.

A summary of the number of high users and the total number of records for each fiscal year is provided in Table 3. There is a larger proportion of high users in FY2014, 0.063, than in FY2015, 0.041. Treating the two years' worth of Puget Sound data as samples from hypothetical FY2014 and FY2015 populations the large-sample test of the null hypothesis that the two years' proportions are equal, is rejected with a p-value of 0.0006. We do not know why the proportions are different. There may have been a change in how opioids are prescribed at the Puget Sound MTFs however there is no evidence of policy changes that may have affected these numbers.

Table 3. Number of High Users for Each Fiscal Year

| Risk File Source | Hi User | Non-Hi User | Total |
|---|---|---|---|
| FY2014 | 177 | 2654 | 2831 |
| FY2015 | 153 | 3539 | 3692 |

The two files, one for each fiscal year are re-combined into a single file. To ensure that this final data set only has unique pseudo IDs, the same merging process is used. For the 843 patients with records in the FY2014 and FY2015 risk files, the larger value of each explanatory variable is used, resulting in a data set with 5680 total patients.

## B. TRAINING AND TEST SETS

We randomly split our data into training and test sets, with 75% for the training set and 25% for the test set. The training set is used (in Chapter IV) to fit a number of different types of models, from which we will choose the "best." The test set is set aside until after the model fitting is complete and used to obtain unbiased estimates of measures of model performance. Selection of the training and test sets is stratified by non-high and high users so that the same ratio of high users is found in both the training and the test set. Table 4 summarizes the number of opioid users in the training and test sets.

Table 4. Number of High and Non-High Users in the Training and Test Sets

| | Training Set | Test Set | Total |
|---|---|---|---|
| High User | 176 | 59 | 235 |
| Non-High User | 4083 | 1362 | 5445 |
| Total | 4259 | 1421 | 5680 |

## C. RESPONSE AND EXPLANATORY VARIABLES

The response variable used in the analysis for the models is binary: 1 indicating a high user of opioids and 0 if not. The criteria for determining whether a patient is a high opioid user follows BUMED's adopted definition of five or more dispensing events of a medication likely to be associated with pain during a 90-day period. This indicator response variable is generated from the PDTS and merged with the risk file according to the pseudo IDs.

There are 88 variables eventually used in the analysis to fit the models. The presence of medical risk conditions make up 77 of the variables. Appendix B lists these medical risk conditions. These conditions are selected directly from the M2 health risk conditions category file. The risk conditions in M2 are based on the Wakely Risk Assessment (WRA) model that maps over 17,000 International Classification of Diseases (ICD) volume 9 diagnosis codes to 90 condition categories (Mehmud, 2012). Appendix C lists the WRA condition categories. BUMED selected 66 of the 90 condition categories that may be relevant to this study. These are shown in Appendix C. The M2 medical conditions file contains 13 sub-categories not included in the WRA, that better reflect the military population's common illnesses. These are annotated in Appendix B and mostly pertain to mental health conditions like PTSD, neurotic disorders and disturbance of conduct. Additionally, the following medical conditions were eliminated as possible factors to simplify our model because no patient in the data set possessed these diagnoses:

- Cystic fibrosis
- Disease of the blood (high)
- Neoplasm cancer (very high)

The eleven variables describe patient characteristics as well as the five possible sources of a prescription. The additional six patient characteristics include a categorical variable for age, presence of acute reaction to stress, a risk score, number of days since most recent Overseas Contingency Operation (OCO) deployment, a binary variable indicating if the individual was ever-deployed and a case management (CM) acuity level. Based on related studies, there are indications that some of these characteristics may affect a patient's opioid usage (Seal, 2014).

## D. DESCRIPTIVE STATISTICS

A brief description and basic statistics for the explanatory variables and their relationship to the response variable is in this section. These include the patient characteristic variables, the five prescription source variables and a handful of medical risk diagnoses variables. Because the exploratory analysis is part of the model fitting processes, the analysis in this section is based only on the 4259 entries of the training set.

### (1) Age Group Category

Rather than give an age in years, the exploratory variable "Age Group Category," taken directly from the M2 risk file, assigns a letter code, D–G, to patients whose ages are 18–24, 25–34, 35–44, 45–64, respectively. Table 5 shows the number of high users for each age group. Although Category E has the greatest number of opioid users, patients in Category G have the largest proportion of high users, thus the proportion of high users is increasing with age group. Additionally, the data set contains 51 entries that did not have an assigned code.

Table 5. Percentage of High Users by Age Group Categories

| Ages (Code Category) | Hi User (%) | Non-Hi User (%) | Total |
|---|---|---|---|
| 18-24 (D) | 31(2.7%) | 1138 (97.3%) | 1169 |
| 25-34 (E) | 65(3.7%) | 1699 (96.3%) | 1764 |
| 35-44 (F) | 56 (5.4%) | 982 (94.6% | 1038 |
| 45-64 (G) | 19 (8.0%) | 218 (92.0%) | 237 |
| No Assigned Code | 5 (9.8%) | 46 (90.2%) | 51 |
| Total | 176 (4.1%) | 4083 (95.9%) | 4259 |

### (2) Acute Reaction to Stress

The factor acute reaction to stress takes two values, "yes" and "no." This factor is defined as "a psychological condition arising in response to a terrifying or traumatic event" (Kenny, 2013). These events can range from sexual assaults to extreme experiences from war conflicts. As a result, military personnel can be at greater risk. Only nine entries were assigned this diagnosis as shown in Table 6. Therefore, this factor will not likely influence our model.

Table 6. Percentage of High Users by Acute Reaction to Stress

| Acute Reaction | Hi User (%) | Non-Hi User (%) | Total |
|---|---|---|---|
| Yes | 1 (11.1%) | 8 (88.9%) | 9 |
| No | 175 (4.1%) | 4075 (95.9%) | 4250 |
| Total | 176 (4.1%) | 4083 (95.9%) | 4259 |

### (3) Risk Score

The risk score describes the person's expected relative cost in medical resources based on the diagnoses and drugs accumulated within the reporting period (DHA, 2016). The lower the score, the less risk for the patient. A score of one means the individual is at normal risk. This risk score is not truncated, so there is no upper bound. In the training set, the score ranged from zero to forty seven. Because only 186 patients have a risk score of five or greater, we assign these patients to a single category. Table 7 lists the number and percentage of high users by risk score. Figure 5 shows that as the risk increases, the proportion of high users of opioids also increases. The red lines indicate the standard error bars for the proportion of high users in each risk score category.

Table 7. Percentage of High Users by Risk Score Category

| Risk Score | Hi User (%) | Non-Hi User (%) | Total |
|---|---|---|---|
| 0 | 4 (0.4%) | 1097(99.6%) | 1101 |
| 1 | 56 (2.9%) | 1883 (97.1%) | 1939 |
| 2 | 38 (6.2%) | 578 (93.8%) | 616 |
| 3 | 18(6.4%) | 265 (93.6%) | 283 |
| 4 | 16 (11.9%) | 118 (88.0%) | 134 |
| 5 or greater | 44 (23.7%) | 142 (76.3%) | 186 |
| Total | 176 (4.1%) | 4083 (95.9%) | 4259 |

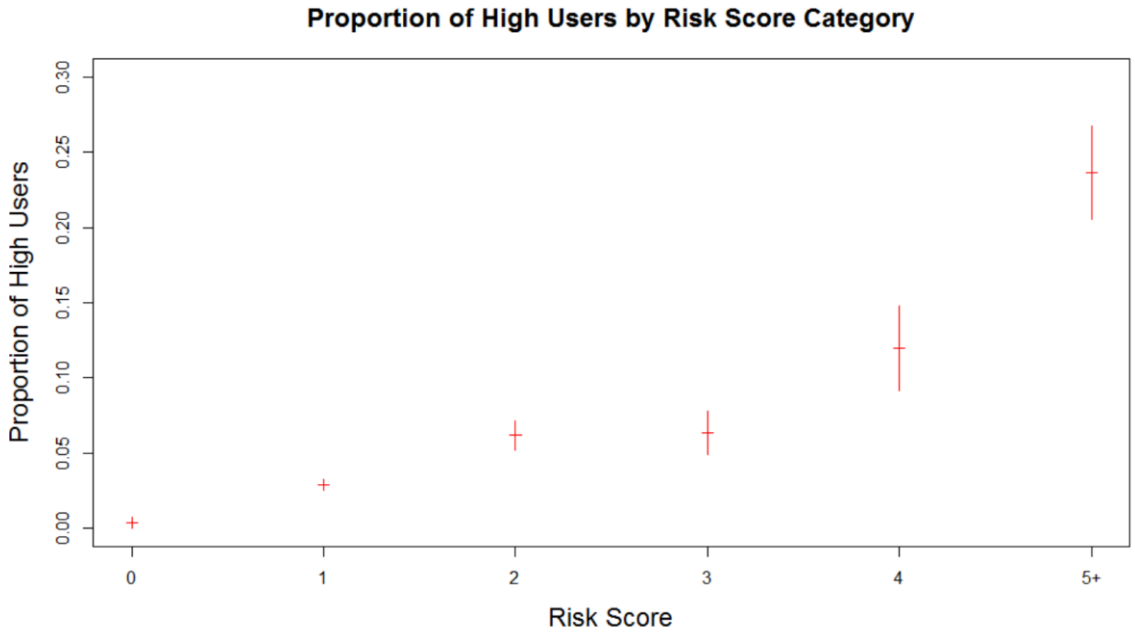


Figure 5. Proportion of High Users in Each Risk Score Category

### (4) Ever Deployed For OCO Deployment

Studies such as Seal (2014) that links opioid use with deployments to Iraq and Afghanistan are not uncommon. While the percentage of high users in Table 8 increases with an OCO deployment, it is only a 1.5% increase.

Table 8. Percentage of High Users by Ever Deployed OCO

| Ever Deployed OCO | Hi User (%) | Non-Hi User (%) | Total |
|---|---|---|---|
| Yes | 113 (4.8%) | 2243 (95.2%) | 2356 |
| No | 63 (3.3%) | 1840 (96.7%) | 1903 |
| Total | 176 (4.1%) | 4083 (95.9%) | 4259 |

### (5) CM Acuity Level

Many patients do not have an assigned CM acuity level, because 91% of patients in the data set have not been assigned a case manager. Case managers assign a score of one to five, with a higher score indicating a patient with more complex health issues, thus requiring greater medical oversight. Appendix D explains the scoring in greater detail. The statistics in Table 9 indicate that there may be a relationship between acuity level and high opioid use as the p-value is 0.0682 based on Fisher's Exact Test (McDonald, 2009).

Table 9. Percentage of High Users by CM Acuity Level

| CM Acuity Level | Hi User (%) | Non-Hi User (%) | Total |
|---|---|---|---|
| 0 | 129 (3.3%) | 3766 (96.7%) | 3895 |
| 1 | 24 (11.1%) | 192 (88.9%) | 216 |
| 2 | 13 (12.0%) | 95 (88.0%) | 108 |
| 3 | 8 (25.8%) | 23 (74.2%) | 31 |
| 4 | 0 (0.0%) | 4 (1.0%) | 4 |
| 5 | 2 (40.0%) | 3 (60%) | 5 |
| Total | 176 (4.1%) | 4083 (95.9%) | 4259 |

### (6) Source of Prescription

There are five prescription source categories, each corresponding to a logical variable that takes value "TRUE" if at least one of the prescriptions for a particular patient comes from that source and value "FALSE" otherwise. The five sources and their codes are:

- D = Direct Care (includes VA mail order pharmacy refills made on behalf of participating MTFs)
- M = Managed Care Support Contractor (MCSC)
- R = Theater Medical Data Store
- T = TRICARE's Mail Order Program
- V = VA CHDR (Clinical/Health Data Repository—Prescription drug information for dual MHS/VA eligible beneficiaries—fully funded by the VA)

The statistics in Table 10 indicate that a majority of high opioid users received their prescriptions from direct care. But a greater percentage of opioid users who receive their medication from the MCSC are high users. Table 10 also shows that the number of high users from the other three sources is quite small.

Table 10. Percentage of High Users by Source of Prescription

| Prescription Source | Hi User (%) | Non-Hi User (%) | Total |
|---|---|---|---|
| D | 170 (4.4%) | 3726 (95.6%) | 3446 |
| M | 87 (11.5%) | 671 (88.5%) | 758 |
| R | 2 (3.1%) | 62 (96.9%) | 64 |
| T | 0 (0.0%) | 2 (1.0%) | 2 |
| V | 1 (25%) | 3 (75%) | 4 |

In the CNA study by Levy et al. (2014), it was noted that patients who received prescriptions from more than one source are more likely to become chronic users. Table 11 examines the relationship between number of source prescriptions and high opioid usage. We also noted that out of the 84 high users that had two or more prescription sources, 82 of those used the direct and MCSC sources. In our models we replace the five binary variables that indicate prescription source with a single variable, number of sources, that takes the value "1" if the number of sources is one and "2" otherwise.

Table 11. Opioid Usage Based on Number of Prescription Sources

| Number of Sources | Hi User (%) | Non-Hi User (%) | Total |
|---|---|---|---|
| One | 92 (2.4%) | 3706 (97.6%) | 3798 |
| Two or More | 84 (18.2%) | 377 (81.8%) | 461 |
| Total | 176 (4.1%) | 4083 (95.9%) | 4259 |

**(7) Medical Diagnoses**

Seal (2014) concluded that there is a link between pain, mental health disorders and PTSD with opioid use. The following seven medical risk diagnoses are examined more closely in Table 12, since these diagnoses can be associated with pain or mental health disorders.

- Anxiety Related Disorders
- Dorsopathy
- Fracture/Dislocation
- Endocrine/Metabolic/Immunity Disorders (EMI)
- Bone/Joint/Muscle Infections/Necrosis (BJMIN)
- Arthropathy
- PTSD

Table 12. Percentage of High Users by Diagnoses

| Diagnoses | Hi User (%) | Non-Hi User (%) | Total |
|---|---|---|---|
| (Y)Anxiety Disorders | 38 (14.7%) | 221 (85.3%) | 259 |
| (N)Anxiety Disorders | 138 (3.5%) | 3862 (96.5%) | 4000 |
| (Y)Dorsopathy High | 41 (20.2%) | 162 (79.8%) | 203 |
| (N)Dorsopathy High | 135 (3.3%) | 3921 (96.7%) | 4056 |
| (Y)Fracture/Dislocation Low | 50 (7.2%) | 640 (92.8%) | 690 |
| (N)Fracture/Dislocation Low | 126 (3.5%) | 3443 (96.5%) | 3569 |
| (Y)EMI Disorder Low | 31 (8.7%) | 324 (91.3%) | 355 |
| (N) EMI Disorder Low | 145 (3.7%) | 3759 (96.3%) | 3904 |
| (Y) BJMIN | 79 (10.7%) | 657 (89.3%) | 736 |
| (N) BJMIN | 97 (2.7%) | 3426 (97.2%) | 3523 |
| (Y)Arthopathy | 80 (8.8%) | 831 (91.2%) | 911 |
| (N)Arthopathy | 96 (2.9%) | 3252 (97.1%) | 3348 |
| (Y) PTSD | 25 (18.1%) | 113 (81.9%) | 138 |
| (N) PTSD | 151 (3.6%) | 3970 (96.3%) | 4121 |

(Y)- Presence of condition

(N)- Absence of condition

Table 12 shows that for all of the above conditions, there is a percentage increase in the number of high users with the presence of the stated condition. The percentage increase varies from 3.7% with the fracture/dislocation condition to 16.9% with the dorsopathy condition. However some of these diagnoses may not have a significant impact in predicting high opioid use due to the low number of patients diagnosed with that condition.

Additionally, since there are 77 medical risk conditions used in the analysis for the model, we explore whether the presence in the number of conditions is related to high opioid usage. The red line in Figure 6 is a loess smoother (see Faraway (2015) for a description of loess smoothers) of the proportion of high users as a function of the number of diagnoses. It depicts an increasing relationship in the proportion of high users as the number of diagnosis conditions increase. The blue dots indicate the proportion of high users with exactly the number of diagnoses. The gray dots in Figure 6 depict the binary response variable with random noise added to both the binary response variable

and the number of diagnoses to avoid overlap of points. Because the relationship between the number of diagnoses and the proportion of high users is so strong, we also include this constructed variable, number of diagnoses in our modeling efforts.

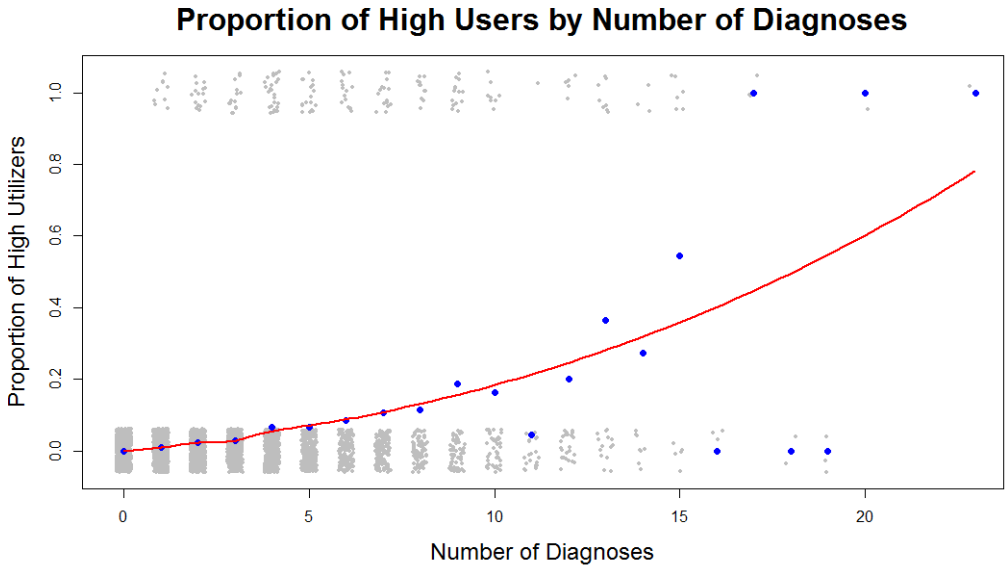


Figure 6. Proportion of High Users by Number of Diagnoses

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# IV. ANALYSIS AND RESULTS

The goal of this chapter is to produce a model to estimate the probability that an opioid-using individual is a high user based on the diagnoses and other variables provided by BUMED and discussed in Chapter III. Estimated probabilities are not intended to be used to classify individuals as high users or not. Instead, they give a score, much like a credit score, to aid health care decisions. This chapter fits four models on the training data set and compares the results. The four models are a basic logistic regression model and three machine learning models: the elastic net penalized logistic regression, the random forest and the boosted tree models. The basic logistic regression model uses only a few explanatory variables selected from those described in Chapter III. It has the advantage of being easy to use and to explain. The machine learning models, on the other hand, make use of all the explanatory variables. Our basic model is compared at the end of this chapter with the best model from the other three methods. For those methods, we vary the parameters and choose the best model within each category type using cross-validated binomial deviance to avoid over-fitting (Hastie, Tibshirani, & Friedman, 2009). We analyze the ROC curves based on the cross-validated predictors to choose the single best model among the three methods and then finally compare it with the basic model. Plotting a lift curve on the test set will allow us to examine unbiased estimates of model performance for the best model for our study.

## A. BASIC MODEL

For our basic high user model, our goal is to create a simple model based on variables that might have the strongest relationship to high opioid use. The standard linear regression model is not appropriate in this study with a binary response variable. Instead, we use logistic regression, which is a generalization of linear regression for binary response variables (Faraway, 2015). Logistic regression models are easily interpretable and are defined as follows: Let $n$ be the number of observations in the training set and model the response variable as independent Bernoulli random variables

where the probability of a "high user," $P_i$ for $i=1,\ldots, n$ is related to the explanatory variables through the log-odds as shown in the following equation:

$$\log\left(\frac{P_i}{1-P_i}\right) = \beta_0 + \beta_1 X_{i1} + \ldots + \beta_k X_{ik},$$

where $X_{i1},\ldots X_{ik}$ are the values of the $k$ explanatory variables for the ith observation and $\beta_0$, $\beta_1,\ldots\beta_k$ are the unknown parameters to be estimated.

Based on Levy et al. (2014), patients who utilized multiple sources for their opioid prescriptions were found more likely to be a chronic user. Further, based on our analysis in Chapter III, the number of diagnoses is strongly related to the proportion of high users. This variable sums the 77 medical risk diagnoses indicator explanatory variables to produce a single variable. Additionally, we consider the explanatory variables of risk score and CM acuity level in developing our basic model. Two variables that we considered, but did not include in our basic model fit are the age group code and the number of days since most recent OCO deployment. Neither variable improved the basic model fit.

In Chapter III, we created two new explanatory variables: the total number of prescription sources and the total number of medical diagnoses for each opioid user. We will begin with a model that includes both of these explanatory variables. The fitted logistic regression model has the form:

$$\log\left(\frac{P}{1-P}\right) = -5.99 + 1.48X_1 + 0.23X_2,$$

where the $P$ is an estimated probability of high use for an individual, $X_1$ is either one, representing one source of prescription or two, representing two or more sources of prescription respectively and $X_2$ represents the total number of diagnoses. The summary statistics for this logistic regression model fit are given in Table 13. The z-values or Wald statistics and corresponding p-values are for a large sample test of the null hypothesis that each coefficient is zero against the two sided test alternative that it is

not (Hastie et al., 2009). There is strong evidence that the coefficient for the number of sources is not zero and the same evidence is true for the other variable, number of diagnoses. Thus, both explanatory variables should be used in our basic model. The null and residual deviance for this model fit are 1466.2 on 4258 degrees of freedom and 1184.3 on 4256 degrees of freedom. The null deviance and the residual deviance are analogous to the total sum of squares and residual sums of squares for linear regression model fits and are often used to compute an R-squared value (Faraway, 2015). Here the R-squared value is 0.24 with the interpretation that only 24% of the null deviance is explained by the logistic regression fit with two variables.

Table 13. Summary Statistics for Logistic Regression with Two Variables

| | Estimated Coefficient | Standard Error (SE) | Wald Statistic | P-value |
|---|---|---|---|---|
| (Intercept) | -5.99 | 0.25 | -23.50 | <0.001 |
| Number of Sources | 1.48 | 0.18 | 8.34 | <0.001 |
| Number of Diagnoses | 0.23 | 0.02 | 11.19 | <0.001 |

The values in Table 13 are on the scale of the log-odds of being a high user. Exponentiating the coefficients yields the odds ratios. Subjects with multiple sources of prescriptions, have nearly 4.5 times the odds of being a high user than those with only one source (Odds Ratio (OR) = 4.4; 95% Confidence Interval (CI) (3.1-6.2)), holding the number of diagnoses constant. Similarly, for every additional diagnosis, there is an increase in odds of being a high user (OR =1.26; 95% CI 1.21-1.31), holding the number of sources constant.

To check that this is a reasonable basic model, we added the interaction between the two explanatory variables, the number of diagnoses and the number of source prescriptions. The large-sample likelihood ratio test (LRT) of the null model without interaction against the alternative with interactions gives a p-value 0.037 with one degree of freedom. There is evidence of interaction at a 5% level of significance, not at a 1% level. With the large sample size, the model with interactions may be statistically

significant but may not be practically significant. There needs to be performance improvement to choose a model with the interaction terms. To see if there is a practical difference in the performance of the two model fits we compare their ROC curves. Common measures of performance used for models with a binary response variable are the true positive rate and false positive rate where an individual is classified as "positive" if the model estimated probability of positive is greater than a specified threshold (0.50 is a typical threshold value). Here positive corresponds to high opioid use. Rather than use a single threshold value, on the training data, the ROC curve considers both the true positive rate and the false positive rate for different threshold levels (James, Witten, Hastie, & Tibshirani, 2013). In Figure 7, the ROC curve for the model with interactions is on top of the curve for the model without interactions. Since the model without interactions is simpler and not notably improved when compared to the model with interactions, out of these two, we will choose the model without interactions.

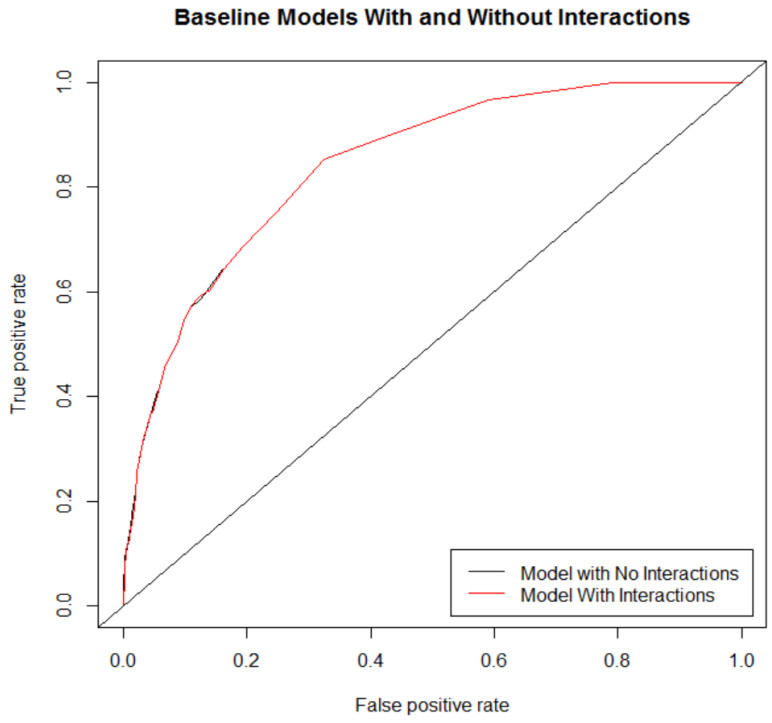


Figure 7. ROC Curves Comparing Models with and without Interactions

To check that the log-odds of high opioid use can be modeled as linear in the number of diagnoses, we converted the explanatory variable, number of diagnoses from numeric to categorical and compared the model fit with our current basic model. The ROC curves for the two models plotted in Figure 8 look very similar, thus the simpler model, based on numeric rather than categorical version of the number of diagnoses variable remains our basic model.

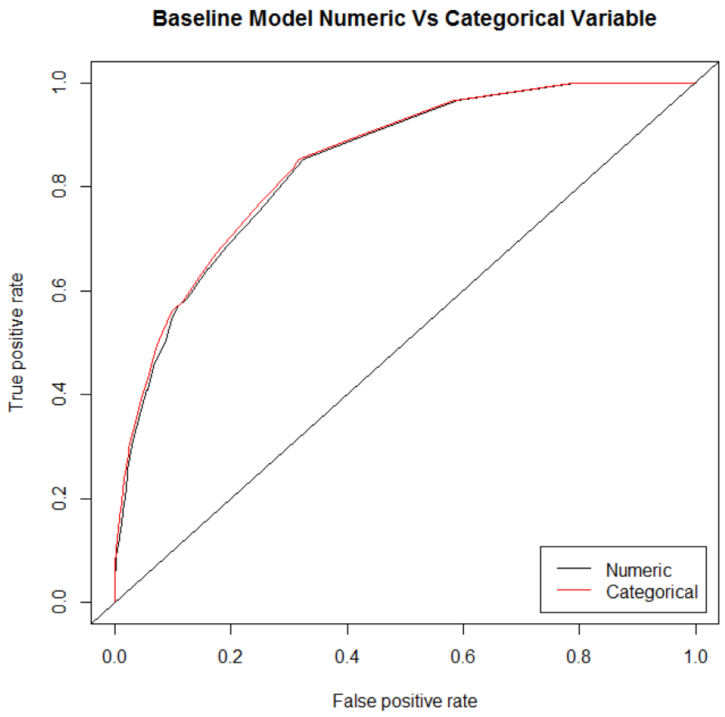


Figure 8. Comparison of Models with Number of Diagnoses Converted to Categorical

Additionally, we explored logistic regression with different combinations of the following four explanatory variables with and without interactions: number of prescription sources, number of diagnoses, risk score and CM acuity level. Similar to the earlier results with using the ROC curve, when we compared each model with our basic model of two variables, our simple model had very similar, if not better results. Thus, for practical purposes, our basic model will contain only two variables: the number of prescription sources and the number of diagnoses with no interactions.

## B. MACHINE LEARNING MODELS

In this section, we compare the three machine learning models: elastic net penalized logistic regression, random forest and boosted trees. For each method, we vary the parameters and use cross-validated binomial deviance to choose the best model within each category type. In order to choose the single best machine learning model, we analyze ROC curves based on cross-validated true positive and false positive rates.

### 1. Elastic Net Penalized Logistic Regression Model

We use a function called *cv.glmnet* to conduct 10-fold cross-validation. This function is part of the **glmnet** package in R (Friedman, Hastie, & Tibshirani, 2010) that fits a regularized generalized linear model via penalized maximum likelihood. In these models, penalties are functions of the magnitudes of the explanatory variables' coefficients. The three choices of penalties are the least absolute shrinkage and selection operator (lasso), $L_1$ absolute value penalty, the ridge regression, $L_2$ quadratic penalty or a combination of the two called the elastic net (Goeman, 2010). How much the likelihood is penalized is governed by a parameter $\lambda$, chosen by cross-validation.

Tibshirani (1996), suggests that an $L_1$ lasso penalty performs better than the ridge penalty when there are a small to moderate number of moderate-sized effects, even out of a large number of explanatory variables. An $L_2$ ridge penalty performs best when there are large number of small effects such as when there is much multi-collinearity among the explanatory variables. The advantage of the lasso penalty is that it acts as a variable selection procedure by shrinking coefficients to zero. A shortcoming for lasso is when a group of variables are highly correlated, it tends to select only one variable from that group.

To use the **glmnet** package, all explanatory variables must be numeric. We converted three categorical variables, CM acuity level, risk score and age group code, to numeric variables. CM acuity levels were consolidated to form a new binary variable, where a "1" represents an individual assigned an acuity level and "0" meant patient was not assigned an acuity level. The age group code variable was converted from categorical with levels "D," "E," "F," "G" to numeric with values 1, 2, 3 and 4

respectively. Lastly, the risk score, with levels 0, 1, 2, 3, 4, 5+ was converted to a numeric variable with values 1 to 6.

To choose the parameter $\lambda$, we compute the cross-validated prediction error for approximately 100 different values of $\lambda$. For cross-validation, we use K=10 randomly-selected folds. The *cv.glmnet* function fits the model to nine folds and then predicts on the remaining fold. This process yields a prediction error, $CV_1$ *and is repeated K-1* times yielding the corresponding *K-1* prediction errors. The average of the ten prediction errors results in *CV*, the cross-validated prediction error in the following equation (Hastie et al., 2009).

$$CV = \frac{\sum_{k=1}^{10} CV_k}{10}$$

We use the Bernoulli (or binomial) deviance as a measure of prediction error. The plot in Figure 9 shows the cross-validated prediction error for the lasso logistic model as a function of log($\lambda$). The left most dotted vertical line shows the $\lambda$ associated with the minimum cross-validated prediction error. The dotted line to the right shows the smallest $\lambda$ within the one standard error (SE) of the minimum cross-validated error. This "one-SE rule" $\lambda$ tends to give a simpler model. The numbers across the top are the corresponding number of variables with non-zero coefficients for that cross-validated prediction error.

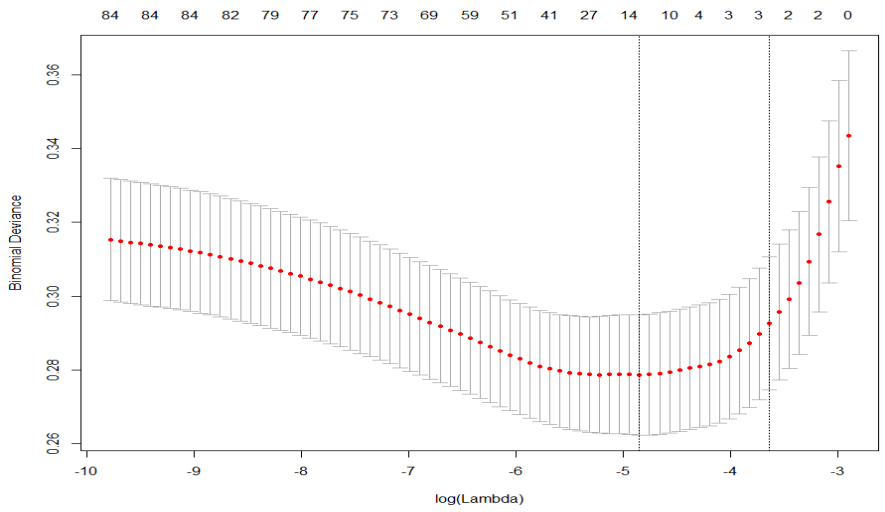


Figure 9. Cross-Validation Error vs. Log($\lambda$) for Binomial GLM

We also penalized the logistic regression models with elastic net penalty. Here the penalty is a combination of lasso and ridge penalties with parameter $\alpha$, where $\alpha$ =1 is a lasso penalty, $\alpha$ = 0 is a ridge penalty and 0< $\alpha$ <1 is a combination of the two. We fit elastic net models varying $\alpha$ from zero to one in increments of 0.1. For each $\alpha$, the one-SE rule $\lambda$, yielded a cross-validated prediction error given in Table 14. The smallest of these is for $\alpha$ = 1 corresponding to a lasso penalty. Thus our best model among the penalized logistic regression models, chosen among models using all possible explanatory variables, is the model with three explanatory variables: the two variables in the basic model and the medical diagnosis dorsopathies high.

Table 14. Lowest CV while Varying $\alpha$.

| $\alpha$ -value | CV |
|---|---|
| 0 | 0.34329 |
| 0.1 | 0.32326 |
| 0.2 | 0.31193 |
| 0.3 | 0.30556 |
| 0.4 | 0.30165 |
| 0.5 | 0.29908 |
| 0.6 | 0.29728 |
| 0.7 | 0.29584 |
| 0.8 | 0.29458 |
| 0.9 | 0.29348 |
| 1 | 0.29261 |

## 2. Tree-Based Models

We fit two machine learning models based on Breiman's (2001) classification trees. See James et al. (2013) for a good discussion of classification trees and related models. For our modeling purposes, the greatest advantage of tree-based models is that they naturally accommodate potential interactions among explanatory variables. In contrast, for logistic regression type models, interactions must be deliberately included as extra explanatory variables. The two tree-based models considered in this section are random forests and boosted trees.

### *a. Random Forest*

Random forests average the outcomes of multiple classification trees (Breiman, 2001). Each tree is fit using a bootstrapped sample taken from the training set and during tree construction only "mtry" number of variables randomly selected from the set of explanatory variables are considered at each split (where mtry is a parameter selected by the user). We use the ***randomForest*** package to fit an initial model, while varying the value of mtry, the number of variables randomly sampled at each split (Liaw & Wiener, 2002). The default value of mtry is the square root of the number of explanatory variables.

This method also produces variable importance measures by averaging the outcomes of the trees. These variable importances explain variation in the response as a function of the explanatory variables. Variable importance provides the average importance of each variable within the model based on the mean decrease in node impurity or gini score (Breiman, 2001). Table 15 lists the most influential explanatory variables in the final random forest model based on gini score. The larger the value, the greater the role that explanatory variable plays in partitioning the data (Witten, Frank, & Hall, 2011). All five of these variables were explored while constructing our basic logistic regression model in Section A.

Table 15. Top Five Influential Variables

| Explanatory Variable | Mean Decrease Gini |
|---|---|
| Number of Diagnoses | 23.9215071 |
| Days Since Most Recent OCO Depl | 23.01504065 |
| Risk Score | 17.51883699 |
| Age Group Code | 15.07520383 |
| Number of Sources | 13.25949064 |

In addition, we use the *train* function from the **caret** package in R to automate searching for the best mtry (Kuhn, 2016). This function returns an object that contains the performance values for each combination of model parameters specified. We use the ten-fold cross-validation to find the model with the lowest cross-validated log-loss (which is proportional to the Bernoulli deviance). Figure 10 suggests that the minimum cross-validated log-loss value occurs between ten to 16 randomly selected explanatory variables.

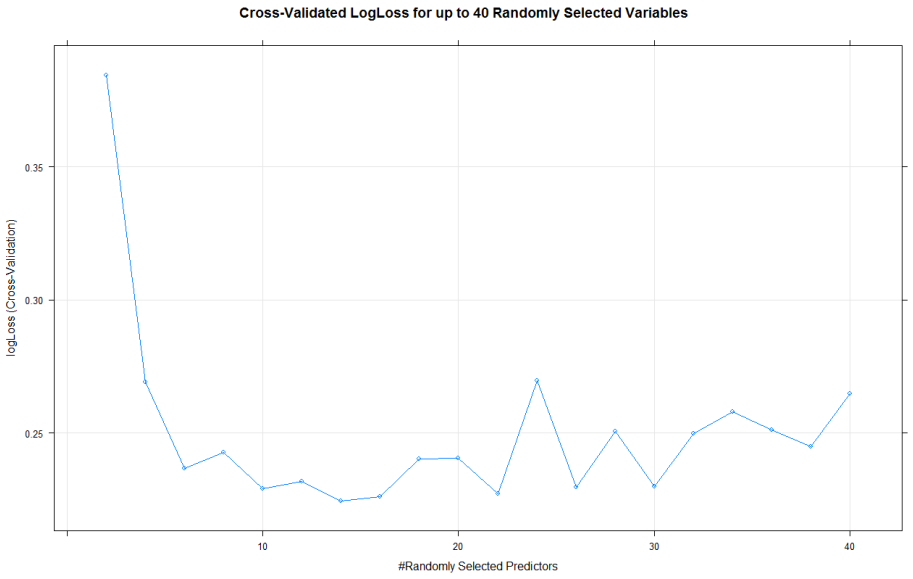


Figure 10. Cross-Validated Log-Loss Based on Number of Variables

We select 14 as our mtry value because it has the smallest cross-validated log-loss according to Table 16. Our random forest model needs to have a sufficient number of trees to ensure every input row gets predicted at least a few times to give good performance and that the classification error stabilizes (James et al., 2013). For this reason, our best random forest model grows 500 trees and randomly selects 14 explanatory variables at each split.

Table 16. Log-Loss for Various Mtry Values

| mtry value | CV Log-loss |
|---|---|
| 2 | 0.3843926 |
| 4 | 0.2690813 |
| 6 | 0.23666 |
| 8 | 0.2426391 |
| 10 | 0.2291392 |
| 12 | 0.2318257 |
| 14 | 0.2244436 |
| 16 | 0.2259266 |
| 18 | 0.2403286 |
| 20 | 0.2405139 |
| 22 | 0.2272155 |
| 24 | 0.2697607 |

***b. Boosted Tree***

Like a random forest model, the boosted tree model is another tree-based model that is a linear function of classification trees. However, it grows incrementally to improve the prediction results (James et al., 2013). This is different from random forest as the growth of a particular tree is influenced by the performance of those that have already been grown. Thus, the trees may not need to be as large and this helps with interpretability. The maximum tree depth corresponds to the potential degree of interaction among explanatory variables. For example, trees with a single split (depth one) are additive with no interactions, trees with depth two can include up to two-way interactions, etc. The trees improve by fitting to the previous residuals instead of to a response variable and continues until a specified number of trees are created (James et al., 2013).

The tuning parameters for boosted tree models are the number of trees, the shrinkage or learning rate, and the interaction depth. We use cross-validation to select an appropriate number of trees as overfitting can occur if this parameter is too large. For the shrinkage parameter, we used a recommended starting value of 0.001 according to James et al. (2013). We varied this parameter up to 0.05 to find combinations of shrinkage parameter and number of trees that could achieve good performance. The third parameter, interaction depth, controls the degree of interaction and adds complexity to the model. For example, an interaction depth of 2 gives a model with up to two-way interactions. e varied this parameter from 1 to 4 and using cross-validation found that complex interactions were not needed.

We use the *gbm* function in R from the **GBM** package to construct our boosted decision tree (Ridgeway, 2015). To choose the optimal model, we use ten-fold cross-validation on the Bernoulli deviance. The three parameters in this model that have the smallest cross-validated Bernoulli deviance are 244 trees, 0.05 shrinkage rate and an interaction depth of two. This model fit suggests that including two-way interactions among the explanatory variables might improve model performance.

## C. COMPARISON OF MODELS BUILT FROM MACHINE LEARNING APPROACHES

ROC curves are used to compare the performance of the three machine learning models in our study: lasso penalized logistic regression, random forests and boosted trees. It appears initially that the random forest and boosted tree models outperformed the lasso penalized regression when analyzing the ROC curves on the training data. Upon further examination, the two tree-based models had over-fit the training data and thus had inflated model performance. Figure 11 shows the random forest ROC curve based on the training set. It indicates that the random forest model can predict high opioid use with almost 100% accuracy on the training set. Unfortunately, these results do not generalize to an independent data set. Therefore, to compare our machine learning models, we plot the cross-validated ROC curves.

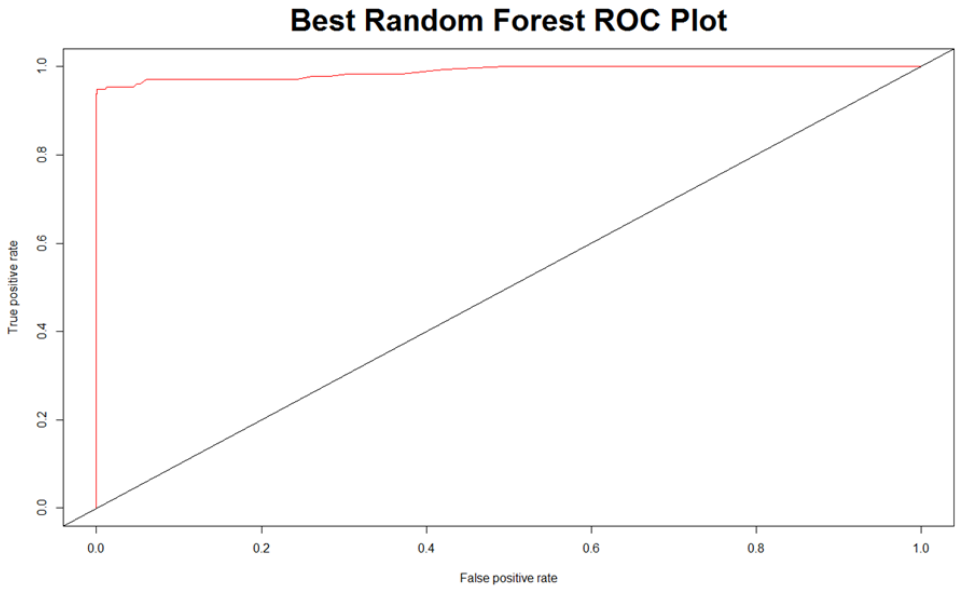


Figure 11. ROC Plot of Over-Fit Random Forest Model on Training Set

Based on Figure 12, the lasso penalized logistic regression and the boosted tree performed similarly well on the cross-validated ROC curve and slightly better than the random forest model. However, because the boosted model uses many trees and all of the explanatory variables, it is comparatively more complex than the lasso penalized

regression. For this reason, our choice for the best machine learning model is the lasso penalized regression. The evaluation of the cross-validated ROC curve performance and model simplicity will be our approach in comparing our best machine learning model with the basic logistic regression model.

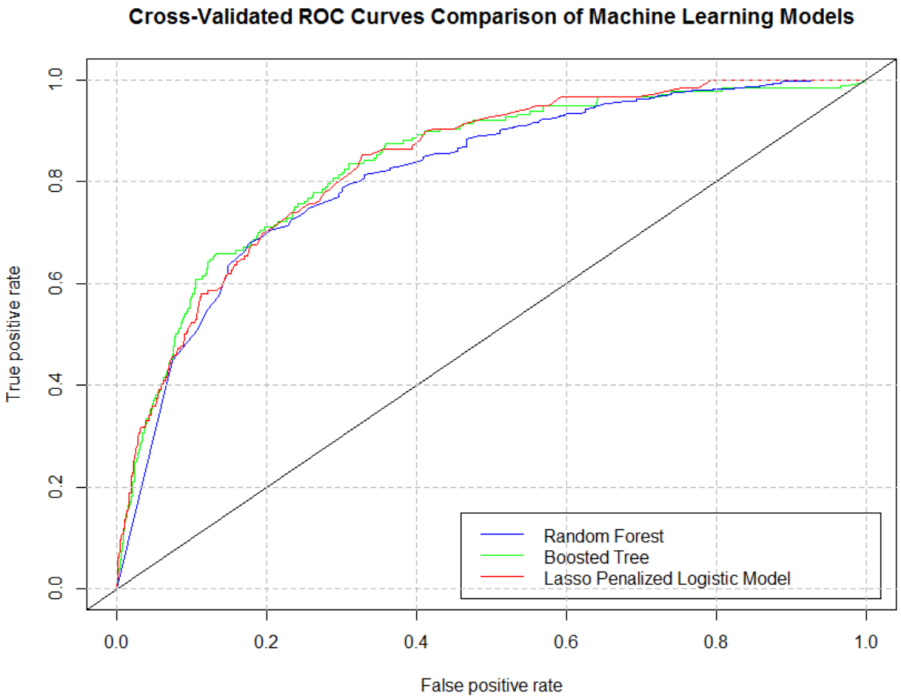


Figure 12. Cross-Validated ROC Curves Comparing Machine Learning Models

## D. RESULTS AND DISCUSSION

In this section, we compare the lasso penalized logistic model with our basic logistic regression model. Figure 13 displays the performance of the two models using their cross-validated ROC curves. There is little difference in ROC curve performance between the two models. So applying the simplistic approach to model selection, the model we recommend for implementation in a health care setting is the simpler logistic regression model. There are a few reasons for this. First and foremost, is easier implementation. A logistic regression with two explanatory factors and with one fewer explanatory variable is easy to replicate and reproduce. The log-odds and probability of a

high user for the logistic regression model are explicit and thus, conceptually, easy to communicate.

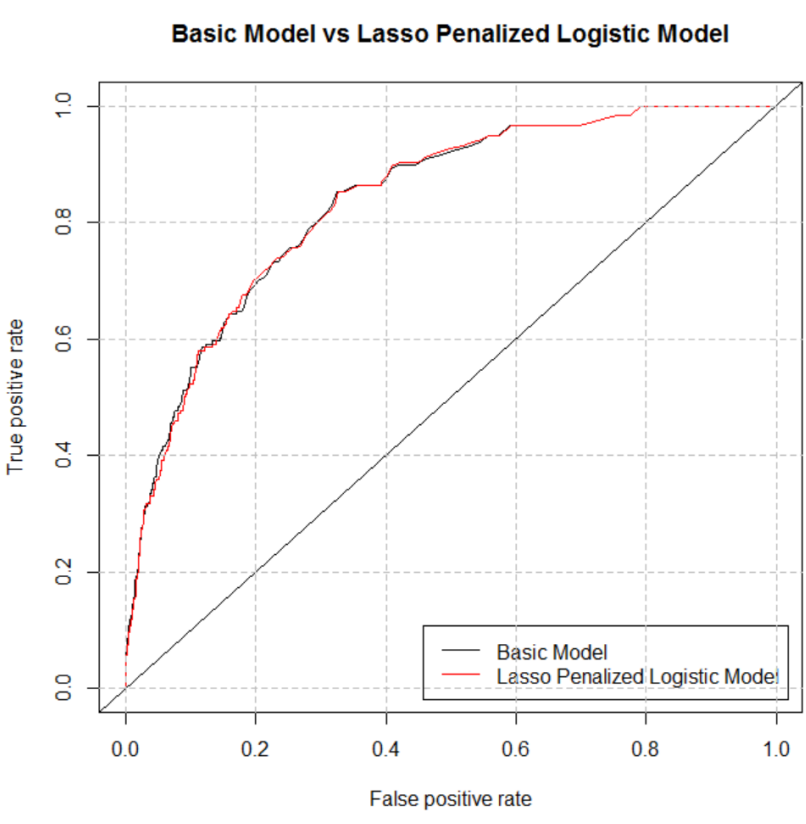


Figure 13. Cross-Validated ROC Curves Comparing Basic Logistic Model with Boosted Tree Regression Model

With the selection of our basic logistic regression model as the preferred model for implementation, we evaluate its performance on the test set and using a more practical approach to evaluate model performance by plotting a lift curve. This is a more functional method to examine how our model performs. Think of the estimated probability of high opioid use (or equivalently, the estimated log-odds) as an individual's score. Now suppose we compute this score for all opioid users in a population, ranking their scores from highest to lowest. If the model is useful the sub-population with the highest scores should have a larger proportion of high opioid users than the proportion of high opioid users in the entire population. Lift is defined as the ratio of the proportion of

high users in the sub-population to the ratio of high users in the general population. The lift plot gives lift as a function of the proportion in the sub-population. Lift curves always reach point (1,1) because by dedicating resources to 100% of the population, the probability of identifying a high user will be the same as the actual probability of high users in the data set (Witten et al., 2011).

Figure 14 shows the lift curve on the test set to analyze model performance. Due to the low number of high users in the test data set, the logistic regression had a lot of variation when the proportion of the total population is less than 0.05. The lift curve goes through the x coordinate at 0.10 and intersects the y coordinate at four, meaning there is a lift of four. In practical terms, by dedicating resources to only 10% of the population, we can now improve and correctly assess the proportion of high users at four times the actual rate. Since the actual percentage of high users in our test set is 4%, we improve our probability of identifying a high user to 16%. Likewise, if we dedicate resources to 50% of the population, the lift is two, meaning the probability of identifying a high user is doubled. So depending on how well we want to assess the proportion of high users or how much resources we have available for use, we can vary the certain threshold sub-population to increase our probability of identifying a high user.

We should note that the lift plot in Figure 14 only shows as an estimate of model performance. However, it illustrates how a model like the basic model might be useful in practice. In the next chapter we outline how our modeling efforts can be improved to be used as an operational health care tool.

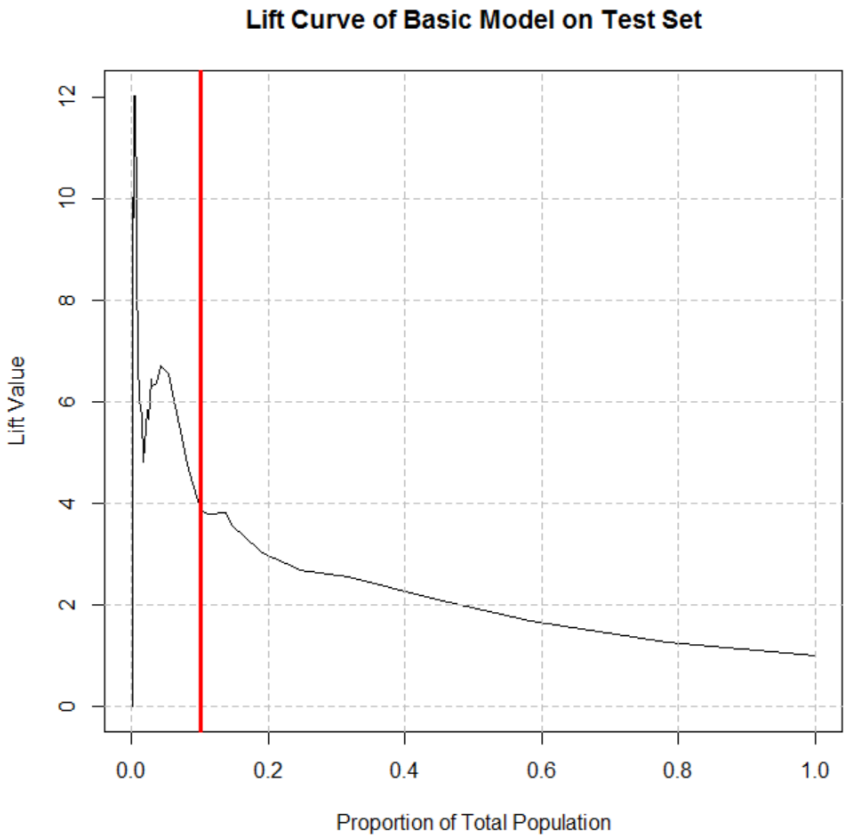


Figure 14. Lift Curve of the Basic Logistic Regression Model on the Test Set

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# V. CONCLUSIONS AND RECOMMENDATIONS

Our goal for this thesis is to examine opioid users in the AD military population and to build a model that estimates the probability that an opioid-using individual is a high user as defined by BUMED. In order to build a good performing model, we had to examine many explanatory variables that potentially influence an individual's opioid use. Our approach was to select, if possible, a simple, executable model and as a result, we reduced the initial 91 variables down to two.

The model that we recommend is a logistic regression model with two explanatory variables, with no interactions. Those two variables are the number of prescription sources for the opioid medications and the total number of diagnoses from the M2 risk file. Although simpler, this model performed well when compared to the more complex machine learning models.

This logistic regression model has the potential to benefit Navy Medicine to make important decisions for their opioid prescribed patients. The tool estimates the probability that an opioid user is a high user. With this information, health care leaders can better plan and manage finite resources to focus on the prevention and treatment of the higher risk patients. This concentrated coordination of care results in improved patient care for this sub-population, reduced long term cost for the military health care system and overall, a more medically ready military force.

Due to the limited demographics data (for example, gender is not included among our explanatory variables) and time period of the data set, spanning only two years, there are factors associated with high opioid users that may not be accounted for. Additionally, the nature of military jobs involves changing duty stations and MTF assignments every few years. The fact that we are only observing AD assigned to the Puget Sound area clinics means that high opioid users that change enrollment sites away from those clinics are under-represented. It also means that AD assigned to Puget Sound might not represent a cross-section of the general Navy population. Lastly, the study analyzed AD patients who were already prescribed opioids to examine factors that can contribute to

high opioid use. This excludes data for analysis of the majority of the AD patients who were not prescribed opioids.

For this reason, a suitable follow-on study could examine data on patients that did not have opioids prescribed to compare the risk factors of becoming an opioid user. The follow-on study should also consider a number of other explanatory variables such as gender and type of duty and be expanded to include other MTFs. Further, if complete records of opioid prescription use are not available because patients change duty stations, then dates a patient enrolls and dis-enrolls from the MTF must be included. With that said, this research is simply an initial effort to explore ways to identify opioid prescribed patients that may have greater risk of becoming a high opioid user.

# APPENDIX A. CANCER DIAGNOSIS CODES

The following table lists the codes associated with cancer diagnosis (Ellis, 2015).

| |
|---|
| **Cancer of head and neck** |
| 1400 1401 1403 1404 1405 1406 1408 1409 1410 1411 1412 1413 1414 1415 1416 1418 1419 1420 1421 1422 1428 1429 1430 1431 1438 1439 1440 1441 1448 1449 1450 1451 1452 1453 1454 1455 1456 1458 1459 1460 1461 1462 1463 1464 1465 1466 1467 1468 1469 1470 1471 1472 1473 1478 1479 1480 1481 1482 1483 1488 1489 1490 1491 1498 1499 1600 1601 1602 1603 1604 1605 1608 1609 1610 1611 1612 1613 1618 1619 1950 2300 2310 V1001 V1002 V1021 |
| **Cancer of esophagus** |
| 1500 1501 1502 1503 1504 1505 1508 1509 2301 V1003 |
| **Cancer of stomach** |
| 1510 1511 1512 1513 1514 1515 1516 1518 1519 20923 2302 V1004 |
| **Cancer of colon** |
| 1530 1531 1532 1533 1534 1535 1536 1537 1538 1539 1590 20910 20911 20912 20913 20914 20915 20916 2303 V1005 |
| **Cancer of rectum and anus** |
| 1540 1541 1542 1543 1548 20917 2304 2305 2306 79670 79671 79672 79673 79674 79676 V1006 |
| **Cancer of liver and intrahepatic bile duct** |
| 1550 1551 1552 2308 V1007 |
| **Cancer of pancreas** |
| 1570 1571 1572 1573 1574 1578 1579 |
| **Cancer of other GI organs; peritoneum** |
| 1520 1521 1522 1523 1528 1529 1560 1561 1562 1568 1569 1580 1588 1589 1591 1598 1599 20900 20901 20902 20903 2307 2309 V1000 V1009 |
| **Cancer of bronchus; lung** |
| 1622 1623 1624 1625 1628 1629 20921 2312 V1011 |
| **Cancer; other respiratory and intrathoracic** |
| 1620 1630 1631 1638 1639 1650 1658 1659 2311 2318 2319 V1012 V1020 V1022 |
| **Cancer of bone and connective tissue** |
| 1700 1701 1702 1703 1704 1705 1706 1707 1708 1709 1710 1712 1713 1714 1715 1716 1717 1718 1719 |
| **Melanomas of skin** |
| 1720 1721 1722 1723 1724 1725 1726 1727 1728 1729 V1082 |
| **Other non-epithelial cancer of skin** |
| 1730 17300 17301 17302 17309 1731 17310 17311 17312 17319 1732 17320 17321 17322 17329 1733 17330 17331 17332 17339 1734 17340 17341 17342 17349 1735 17350 17351 17352 17359 1736 17360 17361 17362 17369 1737 17370 17371 17372 17379 1738 17380 17381 17382 17389 1739 17390 17391 17392 17399 20931 20932 20933 20934 20935 20936 2320 2321 2322 2323 2324 2325 2326 2327 2328 2329 V1083 |
| **Cancer of breast** |
| 1740 1741 1742 1743 1744 1745 1746 1748 1749 1750 1759 2330 V103 |
| **Cancer of uterus** |
| 179 1820 1821 1828 2332 V1042 |

| |
|---|
| **Cancer of cervix** |
| 1800 1801 1808 1809 2331 7950 79506 V1041 79501 79502 79503 79504 |
| **Cancer of ovary** |
| 1830 V1043 |
| **Cancer of other female genital organs** |
| 181 1832 1833 1834 1835 1838 1839 1840 1841 1842 1843 1844 1848 1849 2333 23330 23331 23332 23339 79516 V1040 V1044 |
| **Cancer of prostate** |
| 185 2334 V1046 |
| **Cancer of testis** |
| 1860 1869 V1047 |
| **Cancer of other male genital organs** |
| 1871 1872 1873 1874 1875 1876 1877 1878 1879 2335 2336 V1045 V1048 V1049 |
| **Cancer of bladder** |
| 1880 1881 1882 1883 1884 1885 1886 1887 1888 1889 2337 V1051 |
| **Cancer of kidney and renal pelvis** |
| 1890 1891 20924 V1052 V1053 |
| **Cancer of other urinary organs** |
| 1892 1893 1894 1898 1899 2339 V1050 V1059 |
| **Cancer of brain and nervous system** |
| 1910 1911 1912 1913 1914 1915 1916 1917 1918 1919 1920 1921 1922 1923 1928 1929 V1085 V1086 |
| **Cancer of thyroid** |
| 193 25802 25803 V1087 |
| **Hodgkin`s disease** |
| 20100 20101 20102 20103 20104 20105 20106 20107 20108 20110 20111 20112 20113 20114 20115 20116 20117 20118 20120 20121 20122 20123 20124 20125 20126 20127 20128 20140 20141 20142 20143 20144 20145 20146 20147 20148 20150 20151 20152 20153 20154 20155 20156 20157 20158 20160 20161 20162 20163 20164 20165 20166 20167 20168 20170 20171 20172 20173 20174 20175 20176 20177 20178 20190 20191 20192 20193 20194 20195 20196 20197 20198 V1072 |
| **Non-Hodgkin`s lymphoma** |
| 20000 20001 20002 20003 20004 20005 20006 20007 20008 20010 20011 20012 20013 20014 20015 20016 20017 20018 20020 20021 20022 20023 20024 20025 20026 20027 20028 20030 20031 20032 20033 20034 20035 20036 20037 20038 20040 20041 20042 20043 20044 20045 20046 20047 20048 20050 20051 20052 20053 20054 20055 20056 20057 20058 20060 20061 20062 20063 20064 20065 20066 20067 20068 20070 20071 20072 20073 20074 20075 20076 20077 20078 20080 20081 20082 20083 20084 20085 20086 20087 20088 20200 20201 20202 20203 20204 20205 20206 20207 20208 20210 20211 20212 20213 20214 20215 20216 20217 20218 20220 20221 20222 20223 20224 20225 20226 20227 20228 20270 20271 20272 20273 20274 20275 20276 20277 20278 20280 20281 20282 20283 20284 20285 20286 20287 20288 20290 20291 20292 20293 20294 20295 20296 20297 20298 V1071 V1079 |

| Leukemias |
| --- |
| 20240 20241 20242 20243 20244 20245 20246 20247 20248 2031 20310 20311 20312 2040 20400 20401 20402 2041 20410 20411 20412 2042 20420 20421 20422 2048 20480 20481 20482 2049 20490 20491 20492 2050 20500 20501 20502 2051 20510 20511 20512 2052 20520 20521 20522 2053 20530 20531 20532 2058 20580 20581 20582 2059 20590 20591 20592 2060 20600 20601 20602 2061 20610 20611 20612 2062 20620 20621 20622 2068 20680 20681 20682 2069 20690 20691 20692 2070 20700 20701 20702 2071 20710 20711 20712 2072 20720 20721 20722 2078 20780 20781 20782 2080 20800 20801 20802 2081 20810 20811 20812 2082 20820 20821 20822 2088 20880 20881 20882 2089 20890 20891 20892 V1060 V1061 V1062 V1063 V1069 |
| **Multiple myeloma** |
| 2030 20300 20301 20302 2038 20380 20381 20382 |
| **Cancer; other and unspecified primary** |
| 1640 1641 1642 1643 1648 1649 1760 1761 1762 1763 1764 1765 1768 1769 1900 1901 1902 1903 1904 1905 1906 1907 1908 1909 1940 1941 1943 1944 1945 1946 1948 1949 1951 1952 1953 1954 1955 1958 20230 20231 20232 20233 20234 20235 20236 20237 20238 20250 20251 20252 20253 20254 20255 20256 20257 20258 20260 20261 20262 20263 20264 20265 20266 20267 20268 20922 20925 20926 20927 2340 2348 2349 7951 79510 79511 79512 79513 79514 V1029 V1081 V1084 V1088 V1089 V109 V1090 V1091 V711 |
| **Secondary malignancies** |
| 1960 1961 1962 1963 1965 1966 1968 1969 1970 1971 1972 1973 1974 1975 1976 1977 1978 1980 1981 1982 1983 1984 1985 1986 1987 19881 19882 19889 20971 20972 20973 20974 51181 78951 |
| **Malignant neoplasm without specification of site** |
| 1990 1991 1992 20920 20929 20930 20970 20975 20979 |
| **Neoplasms of unspecified nature or uncertain behavior** |
| 2350 2351 2352 2353 2354 2355 2356 2357 2358 2359 2360 2361 2362 2363 2364 2365 2366 2367 23690 23691 23699 2370 2371 2372 2373 2374 2375 2376 2377 23770 23771 23772 23773 23779 2379 2380 2381 2382 2383 2384 2385 2386 2387 23871 23872 23873 23874 23875 23876 23877 23879 2388 2389 2390 2391 2392 2393 2394 2395 2396 2397 2398 23981 23989 2399 |
| **Maintenance chemotherapy; radiotherapy** |
| V580 V581 V5811 V5812 V661 V662 V671 V672 |
| **Benign neoplasm of uterus** |
| 2180 2181 2182 2189 2190 2191 2198 2199 |
| **Other and unspecified benign neoplasm** |
| 20940 20941 20942 20943 20950 20951 20952 20953 20954 20955 20956 20957 20960 20961 20962 20963 20964 20965 20966 20967 20969 2100 2101 2102 2103 2104 2105 2106 2107 2108 2109 2110 2111 2112 2113 2114 2115 2116 2117 2118 2119 2120 2121 2122 2123 2124 2125 2126 2127 2128 2129 2130 2131 2132 2133 2134 2135 2136 2137 2138 2139 2140 2141 2142 2143 2144 2148 2149 2150 2152 2153 2154 2155 2156 2157 2158 2159 2160 2161 2162 2163 2164 2165 2166 2167 2168 2169 217 220 2210 2211 2212 2218 2219 2220 2221 2222 2223 2224 2228 2229 2230 2231 2232 2233 22381 22389 2239 2240 2241 2242 2243 2244 2245 2246 2247 2248 2249 2250 2251 2252 2253 2254 2258 2259 226 2270 2271 2273 2274 2275 2276 2278 2279 22800 22801 22802 22803 22804 22809 2281 2290 2298 2299 V1272 |

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# APPENDIX B. LIST OF 91 EXPLORATORY VARIABLES

| **Age.Group.Code*** | **Neoplasm.Cancer..High.** |
|---|---|
| Acute.Reaction.to.Stress* | Neoplasm.Cancer..Very.High. |
| Risk.Score..No.Truncation* | Non.Psychotic.Disorders.of.Childhood |
| Days.Since.Most.Recent.OCO.Depl* | Osteoarthrosis |
| Ever.Deployed.Flag..OCO.* | Oth.Musculoskel.Sys..and.Connective.Tissue |
| Anxiety.Related.Disorders | Other.Congenital.Anomalies |
| Arthropathy | Other.Digestive.System.Diseases |
| Asthma++ | Other.Injury..Low. |
| Bone.Joint.Muscle.Infections.Necrosis | Other.Injury..Med. |
| Cardiac..High..Rx | Other.Injury..High. |
| Case.Management.Acuity.Level* | Other.Mycoses |
| Central.Nervous.System..Low. | Other.Neurotic.Disorders++ |
| Central.Nervous.System..High. | Other.Non.Psychotic.Depressive.Disorders++ |
| Cerebrovascular.Disease | Other.Non.Psychotic.Disorders++ |
| Chronic.Ulcer.of.Skin..Except.Decubitus. | Other.Psychotic.Disorders++ |
| Circulatory.Cardiovascular..Low. | Personality.Disorders |
| Circulatory.Cardiovascular..Med. | Polyneuropathy |
| Circulatory.Cardiovascular..High. | Psychotic.Disorders.of.Childhood++ |
| Circulatory.Cardiovascular..Very.High. | PTSD++ |
| Congestive.Heart.Failure | Pulmonary.Respiratory..Low. |
| CP..Hemorrhage..Other.Paralytic.Syn | Pulmonary.Respiratory..Med. |
| Diabetes | Pulmonary.Respiratory..High. |
| Cystic.Fibrosis | Quadriplegia..Other.Extensive.Paralysis |
| Diseases.of.the.Blood..Low. | Renal.Failure..Low. |
| Diseases.of.the.Blood..Med. | Renal.Failure..Med. |
| Diseases.of.the.Blood..High. | Renal.Failure..High. |
| Diseases.of.the.Breast | Respirator.Arrest.Dependence.Trach.Stat |
| Diseases.of.Ear.Mastoid.Process | Schizophrenic.Disorder |
| Diseases.of.Genitourinary.System | Seizure.Disorders.and.Convulsions |
| Disorders.of.Immunity | Seretonin.3.Receptor.Antagonist.Rx++ |
| Disorders.of.the.Eye.and.Adnexa | Skin.and.Subcutaneous.Tissue..Low. |
| Disturbance.of.Conduct++ | Skin.and.Subcutaneous.Tissue..Med. |
| Dorsopathies..Low. | Skin.and.Subcutaneous.Tissue..High. |
| Dorsopathies..High. | Substance.Dependence |
| Endocrine..Metabolic..Immune.Dis..Low. | Substance.Abuse++ |
| Endocrine..Metabolic..Immune.Dis..High. | Substance.Induced.Mental.Disorders++ |

| **Age.Group.Code*** | **Neoplasm.Cancer..High.** |
|---|---|
| Fracture.Dislocation..Low. | Traumatic.Brain.Injury..Low.++ |
| Fracture.Dislocation..Med. | Traumatic.Brain.Injury..High.++ |
| Fracture.Dislocation..High. | Vert.Fractures..Spinal.Cord.Dis.Injury |
| GI.Infectious.Parasitic..Low. | Vascular.Disease |
| GI.Infectious.Parasitic..Med. | D_bool* |
| GI.Infectious.Parasitic..High. | M_bool* |
| Maj.CC.of.Medical.Care.and.Trauma | R_bool* |
| Multiple.Sclerosis | T_bool* |
| Neoplasm.Cancer..Low. | V_bool* |
| Neoplasm.Cancer..Med. | |

* Denotes variables added that are not part of the M2 medical risk conditions.

++ Denotes variables not in the WRA model.

# APPENDIX C. MEDICAL CONDITION CATEGORIES IN WRA MODEL

The following table lists the 90 condition categories in the Wakely Risk Assessment Model (Mehmud, 2012).

| **WRA Category Description** | **WRA#** |
|---|---|
| Arthropathies | WRA1 |
| Bone/Joint/Muscle Infections/Necrosis | WRA2 |
| Central Nervous System | WRA3 |
| Central Nervous System (H) | WRA4 |
| Cerebral Palsy, Hemorrhage and Other Paralytic Syndromes | WRA5 |
| Cerebrovascular Disease | WRA6 |
| Chronic Ulcer of Skin, Except Decubitus | WRA7 |
| Circulatory/Cardiovascular (H) | WRA8 |
| Circulatory/Cardiovascular (L) | WRA9 |
| Circulatory/Cardiovascular (M) | WRA10 |
| Cirrhosis of Liver* | WRA11 |
| Congestive Heart Failure | WRA12 |
| Cystic Fibrosis | WRA13 |
| Diabetes with Ophthalmologic or Unspecified Manifestation | WRA14 |
| Diabetes with Renal or Other Specified Manifestation | WRA15 |
| Diabetes without Complication | WRA16 |
| Dialysis Status* | WRA17 |
| Diseases of the Blood (H) | WRA18 |
| Diseases of the Blood (L) | WRA19 |
| Diseases of the Blood (M) | WRA20 |
| Diseases of the Blood (VH) | WRA21 |
| Diseases of the Ear/Mastoid Process | WRA22 |
| Diseases of the Genitourinary System | WRA23 |
| Disorders of Immunity | WRA24 |
| Disorders of the Eye & Adnexa | WRA25 |
| Dorsopathies | WRA26 |
| Dorsopathies (H) | WRA27 |
| Drug/Alcohol Psychosis or Dependence | WRA28 |
| Endocrine, Metabolic, and Immunity Disorders | WRA29 |
| Endocrine, Metabolic, and Immunity Disorders (H) | WRA30 |
| End-Stage Liver Disease* | WRA31 |
| EXCL* | WRA32 |

| **WRA Category Description** | **WRA#** |
|---|---|
| Fracture/Dislocation | WRA33 |
| Gastrointestinal/Infectious/Parasitic (H) | WRA34 |
| Gastrointestinal/Infectious/Parasitic (L) | WRA35 |
| Gastrointestinal/Infectious/Parasitic (M) | WRA36 |
| HIV/AIDS* | WRA37 |
| Inflammatory Bowel Disease* | WRA38 |
| Injury/Poisoning | WRA39 |
| Lymphatic, Head and Neck, Brain, and Other Major Cancers (H)* | WRA40 |
| Lymphatic, Head and Neck, Brain, and Other Major Cancers (L)* | WRA41 |
| Lymphatic, Head and Neck, Brain, and Other Major Cancers (M)* | WRA42 |
| Major Complications of Medical Care and Trauma | WRA43 |
| Major Depressive, Bipolar, and Paranoid Disorders | WRA44 |
| Major Organ Transplant Status* | WRA45 |
| Mental Disorders | WRA46 |
| Mental Disorders (H) | WRA47 |
| Metastatic Cancer and Acute Leukemia* | WRA48 |
| Multiple Sclerosis | WRA49 |
| Neonate* | WRA50 |
| Neonate (H)* | WRA51 |
| Neoplasm of Bone, Connective Tissue, Skin, & Breast | WRA52 |
| Neoplasm of Bone, Connective Tissue, Skin, & Breast (H) | WRA53 |
| Neoplasm of Digestive/Peritoneum | WRA54 |
| Nephritis* | WRA55 |
| Osteoarthrosis | WRA56 |
| Other Congenital Anomalies | WRA57 |
| Other Digestive System Diseases | WRA58 |
| Other Heart Disease | WRA59 |
| Other Infectious & Parasitic Diseases* | WRA60 |
| Other Infectious & Parasitic Diseases (H)* | WRA61 |
| Other Musculoskeletal System & Connective Tissue | WRA62 |
| Other Mycoses | WRA63 |
| Other Neoplasm | WRA64 |
| Other Pulmonary/Respiratory | WRA65 |
| Other Rare* | WRA66 |
| Other Transplant Related* | WRA67 |
| Parkinson's and Huntington's, other motor control Diseases* | WRA68 |
| Polyneuropathy | WRA69 |
| Pregnancy (Incomplete)* | WRA70 |
| Pregnancy Related* | WRA71 |
| Proliferative Diabetic Retinopathy and Vitreous Hemorrhage* | WRA72 |

| **WRA Category Description** | **WRA#** |
|---|---|
| Protein-Calorie Malnutrition* | WRA73 |
| Pulmonary/Respiratory (H) | WRA74 |
| Pulmonary/Respiratory (L) | WRA75 |
| Pulmonary/Respiratory (M) | WRA76 |
| Quadriplegia, Other Extensive Paralysis | WRA77 |
| Renal Failure (H) | WRA78 |
| Renal Failure (L) | WRA79 |
| Renal Failure (M) | WRA80 |
| Respirator Arrest, Dependence/Tracheostomy Status | WRA81 |
| Rheumatoid Arthritis and Inflammatory Connective Tissue Disease* | WRA82 |
| Schizophrenia | WRA83 |
| Seizure Disorders and Convulsions | WRA84 |
| Septicemia/Shock | WRA85 |
| Skin & Subcutaneous Tissue | WRA86 |
| Skin & Subcutaneous Tissue (H) | WRA87 |
| Vascular Disease | WRA88 |
| Vertebral Fractures, Spinal Cord Diseases/Injury | WRA89 |
| Very Severe Neoplasm / Cancer | WRA90 |

*Denotes medical conditions that were not included in this study.

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# APPENDIX D. CASE MANAGEMENT (CM) ACUITY LEVELS

The information in the following table defines the CM acuity level (DHA, 2016).

| | | | |
|---|---|---|---|
| 1 | Low | 1-150 minutes per month or (0-2.5 hrs per month | Routine discharge planning, minimal intervention(s). |
| 2 | Low to moderate | 151-360 minutes per month or (2.75 - 6.00 hours per month | Stable with ongoing needs, chronic care intervention, infrequent ER/inpatient utilization |
| 3 | Moderate | 361-555 minutes per month or (6.25 - 9.25 hours per month) | Stable with more complicated ongoing needs, frequent ER/inpatient utilization |
| 4 | Moderate to Intense | 556-750 minutes per month or (0.5 - 12.5 hrs per month) | Multiple acute needs |
| 5 | Intense | 751 minutes and above per month (12.75+ hrs per month) | Intensive assessment and/or monitoring required |

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